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THE DEVELOPMENT OF THE THEORY OF CHEMICAL STRUCTURE IN THE WORKS OF V. V. MARKOVNIKOV

(On the 50th Anniversary of His Death)

V. V. Razumovsky

The outstanding Russian chemist, Vladimir Vasilyevich Markovnikov, was born on December 10 (23), 1838, in the village of Chernorechye, not far from Nizhny Novgorod (now Gorky). He received his secondary education in the Nizhegorod Institute for the Nobility. In 1856 Vladimir Vasilyevich entered Kazan University in the Commercial Section of the Faculty of Law. The commercial section gave a broad training both in general knowledge and in natural science.

Chemistry was taught in the commercial section of Kazan University by A.M. Butlerov and technology by M. Ya. Kittary. V. V. Markovnikov developed a special interest in chemistry. While a student of the third course, V. V. Markovnikov wrote down and reproduced by lithography the course of lectures delivered on organic chemistry by A.M. Butlerov in the 1859/60 academic year.

In 1862 he delivered a course of lectures on inorganic chemistry, deputising for the indisposed Butlerov, and in 1863 he delivered a course on analytical chemistry.

In 1863 Vladimir Vasilyevich passed his degree examination and in 1865 he defended his doctoral dissertation on "The isomerism of organic compounds" which played an important part in the development of the theory of chemical structure.

In 1865 Markovnikov went abroad to work in the laboratories of the greatest German chemists of last century – Erlenmeyer in Heidelberg, Kolbe in Leipzig and Baeyer in Berlin. While abroad, he continued to follow the work of his teacher on the theory of chemical structure. V. V. Markovnikov wrote to A. M. Butlerov from Berlin:

"Your researches, as formerly, are very interesting and are evidently moving unerringly toward a solution of the problems you have set yourself" [1]. He was keenly interested in the political life of Germany, about which he wrote as follows in the same letter:

"I should like to go to Switzerland but the direct road is not yet free. The Germans continue to fight but probably not for much longer. After the peace between Prussia and Austria, which will very soon be concluded, it will only remain for the young Germans to submit to the will of Bismarck. The Germans in this town were so carried away by their victories that reasoned discussion with them was out of the question. They imagine that Prussia can now do what she likes and that nobody is in a position to say them nay because nobody else possesses needle guns. . I did not fail to tell my fellow students that they were stupid" [1].

In 1867 Markovnikov returned to Kazan on the occasion of his selection by the University Council as docent of the chair of chemistry. V. V. Markovnikov wrote as follows to Butlerov from Leningrad on March 11, 1867:

"I am very thankful to you, dearest Aleksandr Mikhailovich, for the notification of the successful outcome of my work. I completely lost patience while waiting for your letter and was about to send you a telegram. I myself expected more adverse votes than I received, and for the favorable outcome, as in general for my appointment, I have only you to thank. I think it would be out of place to amplify my expressions of thanks because, of course, you were actuated in this matter principally not by any personal disposition toward myself but by your sense of public duty in relation to the university. It only remains for me to justify the expectations of yourself and the faculty. That the desire to do so is strong, I give you my word of honor – my doubt is as to the adequacy of my talents ... In a few days I shall send a petition to the Ministry for a deferment until October. It is still necessary for me to spend the whole of the summer semester here and to visit Paris. Apart from that I should very much like to attend the congress of chemists" [2].

At the end of December 1867 and the start of January 1868, V. V. Markovnikov took an active part in the work of the first congress of Russian naturalists and doctors in Petersburg under the auspices of the Russian Chemical Society.

Describing the congress to Butlerov, who was abroad on a mission, Markovnikov wrote:

"On the whole the congress could not have been more successful. Everybody appears to be satisfied. Among the papers presented at the sittings, those of Engelhardt and Beilstein were particularly interesting, the former because of its expression of divergence from Kekule's theory...Beilstein dealt with the chlorination of toluene. His method enables gradual substitution of the whole of the hydrogen, either in the methyl or in the phenyl. At will one can also substitute the hydrogen either in the one radical or in the other. He also found that with water chlorotoluene reacts to give benzaldehyde which is already being produced in Berlin by this method from toluene.

"For chemists the congress was useful if only because of the unanimous desire to found a chemical society in Petersburg and the ministry has already promised to authorize it. It is planned to publish the work of Russian chemists as soon as material is communicated...Six of us were at the congress and Kazan in general created an effect! We constantly received thanks for our active participation, and even at the farewell dinner the chairman, after toasting all the universities together, proposed a special one for Kazan University" [3].

In 1868 A. M. Butlerov was chosen as full Professor of the Chair of organic chemistry at Petersburg University. After Butlerov had been transferred to Petersburg, the chair of chemistry was occupied by V.V. Markovnikov. At this period Markovnikov was working out the theory of the mutual influence of atoms in molecules. In 1869 Markovnikov defended his celebrated doctoral dissertation on "Data on the question of the mutual influence of atoms in chemical compounds". In response to the suggestion that the dissertation should be translated into German, Markovnikov declared:

"If the ideas here expounded are of interest, those wishing to do so may make use of this Russian paper" [4].

The pioneer scientist and patriot V.V. Markovnikov all his life defended the priority of Russian science and carried on a fight against the printing of the papers of Russian chemists in foreign languages.

Not only did he himself publish all his papers originally in Russian, but he urged all Russian scientists to do the same. V.V. Markovnikov also put this problem before Butlerov who at that time headed the Petersburg school of chemists:

"Tell me please why all the Petersburg chemists have begun to publish again their work in foreign journals even before they are published in the Russian language? What then is the purpose of our society and journal? I find this completely tactless, and if it continues I shall leave the society" [5].

Markovnikov's patriotism and his active fight for the honor and dignity of Russian science provoked the hostility of scientific opponents, and principally of members of foreign academies. Subsequently this was also clearly manifested in the Academy itself.

The conversation of Markovnikov with the academician Yu. F. Fritsche was characteristic:

"Nothing of any interest was of course to be expected from a meeting with Fritsche. Suddenly he began a conversation about the reproaches made against the Academy for bringing out its bulletin in German, and he naturally defended this policy" [6].

In 1869 Markovnikov was elected extraordinary professor of Kazan University and in 1870 he became ordinary professor. At the same period A.M. Butlerov was elected to the Academy of Sciences and Markovnikov, in a letter of congratulation, expounded his unusual ideas about the value of lectures in a higher educational course:

" However dull lectures may sometimes appear, they have the advantage of allowing one's own ideas to be put forward. This opportunity is not open to any of the academic staff who are not professors because in papers it is inconvenient to say all that one might say at lectures. However small my audience, I can always try out my ideas on them" [7].

In October, 1871, Markovnikov resigned his professorship at Kazan University as a mark of protest against the illegal dismissal of the outstanding Russian scientist and public-spirited worker, the professor of anatomy P. F. Lesgaft.

On this matter Markovnikov wrote as follows in a letter to Butlerov on October 25, 1871: "...You understand that the conditions existing at Kazan University at the present time make it impossible to remain there, and that is why I am compelled to ask you for help in getting away from Kazan. We are definitely convinced that we are in danger because we are surrounded by a network of the darkest and most inadmissible intrigues whose first victim was Lesgaft. The persons known to you are not scrupulous in their methods even if these should lead to unrest among the students..." [8].

At the end of 1871 Vladimir Vasilyevich was chosen as ordinary professor of chemistry of the Novorossiysk University in Odessa. However he spent the 1872/73 academic year in Odessa. At this time, the rectorate of Moscow University, wishing to raise the teaching of chemistry to a high level, invited D. I. Mendeleev to fill the chair of Chemistry. D. I. Mendeleev was closely attached to Petersburg and was compelled "to refuse in honor to give up his work at the oldest Russian university" [9]. In his letter of September 28, 1871 to the dean of the physico-mathematical faculty of Moscow University (A.Yu. Davydov), Mendeleev indicated Markovnikov as the most meritorious candidate for the chair of chemistry. In the summer of 1872 Markovnikov was invited by Davydov to transfer to Moscow University. In 1873 the Council of Moscow University chose Markovnikov as ordinary professor of chemistry.

"During the Science Congress in Moscow in 1869" — we read in Markovnikov's autobiography — "the status of chemistry at this university made an extremely poor impression on all Russian chemists. It was generally considered that chemistry was absent from Moscow" [10].

At Moscow University Markovnikov undertook the enormous task (extending over many years) of organizing and equipping the chemical laboratory and of constructing a new and large laboratory. The number of natural science students wishing to take chemistry under the guidance of Markovnikov steadily increased from year to year. From Markovnikov's laboratory began to be published researches in considerably greater number than from any other Russian chemical laboratory.

At Moscow University Markovnikov founded the most important school of Russian chemists, as represented by: N. Ya. Demyanov, I.A. Kablukov, N. M. Kizhner, M.I. Konovalov, A.E. Chichibabin, A.M. Berkengeim, N.I. Kursanov, Yu. V. Lermontova, V. N. Ogloblin, P.P. Orlov, A.N. Reformatsky, A.P. Sabaneev, A. N. Shchukarev and A.A. Yakovkin.

Vladimir Vasilyevich occupied the chair of analytical and organic chemistry of Moscow University for 20 years (1873-1893). In 1893/1894 the chair was occupied by Professor N.D. Zelinsky.

Markovnikov did not, however, leave Moscow University but continued to work there on a restricted scale right to his end on February 11, 1904. In the last decade of his activity at Moscow University he carried out scientific research and guided several students and co-workers.

A vivid picture of the scientific activity of Markovnikov at Moscow University was drawn by K.A. Timiryazev when commemorating the fortieth year of the scientific activity of the great Russian chemist:

"What chemistry was at Moscow University before you and what it has become, thanks to you, is evident to us. It was certainly no coincidence that in the same period prior to you two scientific papers were published from this laboratory, while in your time the number was two hundred. Nor is it fortuitous that with your arrival in Moscow and the almost simultaneous arrival of A.G. Stoletov as professor of physics, the entire destiny of the natural science section of the mathematical faculty was changed. The number of students which had steadily fallen from 17 to 1 in the forth course, suddenly began to increase to 100 and then to 600-700" [11].

In Moscow University Markovnikov started and completed his classical investigations of Russian petroleum and made the most valuable contributions toward the development of knowledge of the reciprocal influence of atoms.

The 20 years in which Markovnikov studied the chemical nature of Russian petroleum opened up the widest perspectives for the development of the science of petroleum and for the chemical industry. Prior to the investigations of Markovnikov only a few facts were known about the composition of Russian (Caucasian) petroleum and some erroneous statements had been published.

In the laboratory of Moscow University, Markovnikov and his students carried out systematic investigations of the composition of Caucasian petroleums, of the chemical and physical properties of individual fractions: elementary composition, ash content, acidity, optical activity, refractive index and coefficient of expansion. By repeated fractional distillations Markovnikov effected resolution of the fractions of Caucasian petroleums and isolated their narrow cuts. Markovnikov's investigations showed for the first time that the chemical nature of Russian (Caucasian) petroleum was quite different from that of American (Pennsylvanian) oil. He discovered that the main components of Caucasian petroleum were naphthenes (cycloparaffins). The individual hydrocarbons isolated by Markovnikov from Caucasian petroleum proved to be derivatives of cyclohexane and cyclopentane [12].

Markovnikov widened the scope of his petroleum researches by synthesizing numerous naphthenes and their derivatives (naphthenic acids) with the aim of studying the structure of the hydrocarbons of Caucasian petroleum. In his laboratory he synthesized five-, six- and seven-membered polymethylene hydrocarbons.

1,3-Cyclobutanedicarboxylic acid, synthesized for the first time by Markovnikov and G. A. Krestovnikov (1880), was the first synthesis of a carbocyclic system with four carbon atoms in the history of organic chemistry. This investigation of Markovnikov refuted the then widespread idea of the impossibility of existence of four-membered carbon rings. Later (1893) Markovnikov obtained cycloheptane in his laboratory and thus disproved Baeyer's strain theory which postulated the possibility of existence of only five- and six-membered cyclic compounds [13].

The investigations of suberone (cycloheptanone) and its derivatives, which also led the scientist to the discovery of the seven-membered carbon ring, were actually the climax of his experimental activity in chemistry.

Markovnikov approached the study of the dynamics of polymethylene rings and their intramolecular rearrangements on the basis of the theory of the mutual influence of atoms. He studied the isomeric transformations of cycloheptane and cyclohexane hydrocarbons and their derivatives [14]. His study of the molecular rearrangements of polymethylene hydrocarbons led Markovnikov to the notable discovery of the contraction of carbon rings. He observed this phenomenon for the first time in the conversion of a seven-membered into a six-membered ring.

On the suggestion of Markovnikov, his pupil N.M. Kizhner carried out the hydrogenation of benzene and made the important observation of the transformation of benzene into methylcyclopentane [15].

Another pupil, N. Ya. Demyanov, continued Markovnikov's work in the field of the molecular dynamics of cyclic systems and established the fundamental laws of expansion and contraction of polymethylene rings.

In a study of the stability of cyclopentane hydrocarbons, Markovnikov established that the five-membered ring is ruptured under the action of hydriodic acid with formation of paraffins [16].

These discoveries and investigations of Markovnikov predetermined all later investigations and achievments in the chemistry and technology of petroleum down to the present day.

Markovnikov also discovered aromatic hydrocarbons (benzene, toluene, pseudocumene, diethylbenzene, isoamylbenzene, etc.) in Caucasian petroleum.

"My researches with petroleum" — he writes — "are making progress and interesting things are coming to light. It appears that petroleum contains an extraordinary diversity of aromatic hydrocarbons, representing up to 20% of the oil after purification from oxygenated compounds. But each fraction contains very little, and that is why they are very difficult to separate. However, at the next meeting there will probably be something to report" [17].

Markovnikov established the genetic relation between naphthenes and aromatic and aliphatic ("fatty") compounds and discovered their structures and their characteristic chemical reactions [18].

The methods used by V. V. Markovnikov for chemical working-up of the narrow fractions of petroleum (nitration, sulfonation, oxidation, chlorination, iodination, bromination and sulfur-dehydrogenation) enabled him and his pupils to obtain numerous derivatives of petroleum hydrocarbons of enormous value for our national economy and modern chemical industry.

Markovnikov left the study of petroleum to take up the investigation of other natural products.

He said: "I am entirely unable to see anything opprobrious in a Russian professor of chemistry carrying out applied research" [19].

Together with A.N. Reformatsky he studied the composition of rose oil. This investigation brought out more prominently the link between napthenes and terpenes. Markovnikov examined Turkestan manna and isolated a sugar from it [20]. He demonstrated that Turkestan manna is melezitose. A thorough investigation of melezitose was carried out in Markovnikov's laboratory in Moscow University by A.V. Alekhin.

The scientific work of V.V. Markovnikov, combining theory with practice, dominated the Russian conception of chemistry.

In 1884 Markovnikov formed a chemical committee in the physical division of the Society of Naturalists, Anthropologists and Ethnographists, which in 6 years was reorganized into the chemical division of the society. From 1884 to 1904 Markovnikov headed in succession the chemical committee and the chemical division of the Society of Naturalists, which constituted the scientific association of Moscow chemists.

With full reason Markovnikov observed:

"In short I wish to take the liberty to say that only my chemical researches,so to speak, originated in Moscow, as I previously mentioned in my address this year to the chemical division on the occasion of my refusal of the chairmanship" [21].

The Tsarist regime not only did not value the highly fruitful activity of V.V. Markovnikov in Moscow University, but even deprived him of his chair.

With bitterness and anger Markovnikov wrote:

"And what do they tell me in gratitude for all that I have done: Get out of here! You are not needed!" I listen for sympathy from chemists. But does anything happen? On my word as a chemist they put a cross, although I could still work on with profit. Not only am I insulted but also Russian science..." [22].

The great services of V. V. Markovnikov to Russian science enabled Academician A.M. Butlerov, jointly with Academicians N.N. Koksharov and V.G. Imshenetsky on November 9, 1882 to propose his candidature as a corresponding member of the Academy of Sciences in the Chemical Division.

In his presentation Butlerov wrote:

"In his researches Markovnikov has been mainly occupied with phonomena of isomerism of organic substances and with the question of the mutual influence of atoms in chemical compounds. His publications on the first theme deal with: the bromide of allyl alcohol; isobutyric acid, which Markovnikov obtained for the first time, independently of Erlenmeyer- the identity of "acetonic" acid with one of the hydroxybutyric acids; and the isomerism of pyrotartaric acid. All these investigations had great value in clarifying the chemical structure of the compounds mentioned as well as for the theory of structure itself. In the second group of researches we mention in particular those on aliphatic hydroxy acids which greatly aided the elucidation of the laws involved in the substitution of the hydrogen of aliphatic organic compounds and solution of the problem of the order in which the hydrocarbon groups in a molecule are influenced by radicals. Nor has Markovnikov shunned the applications of our science. Thus he participated in the organization of disinfection on the battlefield during the last Eastern War; some of his papers deal with various problems of industry; for some time, in collaboration with one of his pupils (Ogloblin), he has been investigating Caucasian petroleum and has already published many results" [23].

On November 13, 1882 the permanent secretary of the Academy of Sciences K.S. Veselovsky notified Academician A.M. Butlerov that "the agreement of the President to this had not been obtained" [24].

Exactly a year later, A.M. Butlerov with the permission of the President again proposed V.V. Markovnikov as corresponding member in chemistry and particularly stressed the value of his candidate's work on the chemistry of petroleum:

"The investigations of Professor Markovnikov on petroleum, carried out with one of his pupils (Ogloblin), have now been published in detail in an exceptionally long paper and have been acknowledged by the University as worthy of the award of the Ilyenkov Prize" [25].

In connection with his presentation in the Academy of Sciences, Markovnikov wrote to A.M. Butlerov:

"I thank you, dear Aleksandr Mikhailovich and others, for your compliments. I shall naturally not refuse the honor if the Academy elects me a corresponding member and I shall conscientiously try to fulfill my obligations".

"It seems to me, however, that I shall not be granted this honor. They will naturally ask Beilstein for his opinion, and I have not the slightest reason to expect a favorable testimonial from him, judging by his attitude toward me during the exhibition, although outwardly our relations were good. Probably he will recommend the more neutral Zaitsev. By this choice the Academy will escape the embarrassment of being in conflict with you. By the way, about Friedrich (F.F. Beilstein — author). Should I not send to the next meeting of the society several results of work with petroleum which contradict his conclusions? What do you think?" [26].

The reactionary majority of the Academy voted against the great Russian scientist and public worker, as well as against Butlerov's other candidates — A.M. Zaitsev and N.A. Menshutkin — and in their place they elected second-rate German Scientists and even foreign subjects.

This same reactionary majority of the Academy also blackballed the first of Butlerov's candidates as active member of the Russian Academy of Sciences — the great Mendeleev.

In the sixties of the 19th century the central problem of organic chemistry was that of isomerism. Round the problem of isomerism in those years raged the battle for the atomic-molecular theory of the structure of substances, the battle for materialism in chemistry.

Gerrard's mechanistic theory of types proved completely incapable of explaining the numerous phenomena of isomerism in organic chemistry. Gerrard claimed that experiment enabled us only to distinguish past and future substances, but not those actually existing. The irrational views of Gerrard led him to completely reject the concept of the internal structure of a substance, the structure of isomers of molecules.

V. V. Markovnikov in his magisteral dissertation exposed the fundamental errors of Gerrard's theory of types in elucidating the nature of molecules and their isomerism: "Assuming the chemical particle to be an indivisible whole, Gerrard also rejected the possibility of evaluating the internal arrangement of atoms in them with the help of chemical transformations alone...In his opinion, chemistry may study a substance only in the past and future, but the present belongs to physics, for which chemical reactions serve only as an auxiliary in comparing the concepts of the structure of materials. It is agreed that such an opinion, postulated as a basis for the whole of science, could not be fruitful for elucidation of the cause of isomerism" [27].

In this connection, Vladimir Vasilyevich acknowledges the great scientific services of Gerrard in the development and experimental founding of the ideas of Avogadro and Ampere and in the defining of the fundamental concepts of chemistry: "atom", "molecule", "equivalent".

In the course of his work on the development of the theory of chemical structure, Markovnikov wrote that "...the definitions of isomerism and metamerism given by Butlerov do not clearly express the significance of the examples adduced. The following definition will be in perfect accord with the theory of chemical structure. Isomers are substances whose radicals, with identical number of carbon equivalents directly linked with one another, contain the same number of other equivalents differently arranged in relation to the carbon" [27].

Markovnikov's definition of isomerism was later adopted by Butlerov in his classic work —"Introduction to the Complete Study of Organic Chemistry", [28].

Markovnikov's dissertation was permeated by the idea that only the theory of chemical structure can truly explain the cause of isomerism.

Markovnikov wrote: "By applying the concept of chemical structure we can explain the difference in the majority of known cases of isomerism. It is evident that the more complex is a substance, the greater the possibilities for a different grouping of the elements, and consequently also the number of isomers must increase" [27].

Markovnikov brings forward many examples to show that isomerism is the inevitable consequence of a specific order of the chemical bond in atoms and molecules. Referring to the isomerism of saturated alcohols, he established that "the number of isomers increases not only with increasing amount of carbon in a radical, but also with increasing number of non-carbon radicals" [27]. Markovnikov also quite specifically indicates the influence of external conditions on the direction of isomeric transformations of molecules: "It is likewise not improbable that an influence is exerted by the temperature, the reaction energy, and other conditions, as yet little known to us, so that from one and the same alcohol under various conditions we can obtain different isomeric hydrocarbons" [27]. In the search for isomers of molecules, Markovnikov resorted to a profound study of the structure of substances, to an exhaustive examination of the by-products of reactions: "...the large number of so-called by-products has been investigated only superficially. But in part of them is contained the whole diversity of transformed isomeric substances; sometimes only an exhaustive study of all the products formed in identical conditions can give good assistance in establishing whether we are dealing with identical or isomeric substances" [27].

In the 18th century the sole method of study of the composition of a substance was analysis. According to the chemistry of his day, Lavoisier was defined as an analytical chemist. The successes of the analytical method in the study of substances led to the definition of an element as the limit of chemical analysis. In the forties of the 19th century Gerrard proposed the method of double decomposition for the study of the composition of a substance. He assumed that the greater the number of double decompositions that can be expressed by the formula of a substance, the more rational is that formula. As early as the forties of the 18th century (1749), however, Lomonosov had embarked on the study of the composition of substances from a deeply materialistic angle. For the understanding of the nature of a substance he proposed to combine analysis with synthesis. Lomonosov pointed out: "... in chemistry synthesis is often more trustworthy than analysis, and it even suffices in itself to identify components" [29]. By underlining the unity of analysis and synthesis in the understanding of the nature of a substance. Lomonosov discovered new analytical techniques; "...but in association with synthesis analysis endows it with much weight, and itself gains much thereby" [29]. The significance and the role of the experimental method indicated by Lomonosov for the study of composition and structure was fully revealed by materialistic dialectics.

"Chemistry in which the form of the investigation predominates is analysis" — wrote Engels — "but it is worthless without its antithesis (synthesis)" [30].

Summing up a century of the experimental study of the composition and structure of molecules by the chemical method, Butlerov stated:

"Conclusions about the chemical structure of a substance can best be reached in all probability on the basis of study of the methods of their synthetic formation..." [31].

Developing the synthetic trend in chemistry, V. V. Markovnikov carried out an investigation of the synthesis of organic acids. He was the first to synthesize isobutyric acid, whose existence he predicted on the basis of the theory of structure. His investigation demonstrated the fallacy of Erlenmeyer's hypothesis of the structure of butyric acid and its isomer, both of which he regarded as identical.

Markovnikov wrote: "Isobutyric acid is the first example of isomerism in the monobasic fatty acid series" [27].

Markovnikov's researches resolved the problems of the structure and isomerism of hydroxybutyric and bromobutyric acids about which ideas were very confused at that time. Studies in this field by eminent foreign chemists (Wurtz, Frankland and Duppa, Wislicenus and others) were only correctly interpreted after Markovnikov had applied to them the theory of chemical structure. Subsequently Markovnikov studied the structure and isomerism of bromo- and hydroxyisovaleric, hydroxyisocaprylic and pyrotartaric acids. He also studied the structure of allyl bromide and the isomerism of oxygen-containing derivatives of propane in order to demonstrate the accuracy of the predictions of the theory of chemical structure [33].

From a letter by Markovnikov to Butlerov from Heidelberg (1865) we learn that the investigation of the isomerism of valeric acid was among the plans of the young scientist.

The extent to which such projects were among the scientific plans of Markovnikov is evident from the fact that the study carried out by A. M. Butlerov in 1872 of the isomerism of valeric acid led him to the synthesis of a new isomer of valeric acid – trimethylacetic acid.

Problems of structure and isomerism of acids and their derivatives predominantly engaged Markovnikov throughout the whole of his scientific career. Thus in 1874 he wrote as follows from Moscow to Butlerov in Petersburg:

"Would you ask Menshutkin whether he retained in the editorial office my paper on the oxidation of hydroxybutyric acid which I sent from Kazan and did not publish on your advice.

"Now, in view of the appearance of the paper of Popov and Lei on the same topic, it acquires some value, for the facts there described are true. I did not keep a copy and I should like you to send it to me if it has been kept. After suitable modification in the light of the present situation, I intend to publish it" [34].

And in 1875 in the pages of the Journal of the Russion Chemical Society appeared Markovnikov's paper on the products of oxidation of α-hydroxybutyric acid [35].

Markovnikov's discovery of the isomerism of the organic acids, as predicted by the theory of structure, showed that chemical structure provides the key to the scientific clarification of the phenomena of isomerism.

These investigations of Markovnikov played an important part in the strengthening and recognition of the theory of chemical structure.

In Germany Markovnikov was a protagonist of the ideas of the theory of chemical structure in opposition to the views of German chemists. In Heidelberg Markovnikov had fierce debates with Erlenmeyer on the principles of the theory of chemical structure.

Erlenmeyer, Kekule and Kolbe were for many years protagonists of the hypothesis of different units of affinity in atoms. On the basis of this hypothesis the German chemists made serious mistakes in connection with problems of the isomerism of alcohols, ketones and other organic compounds. Kekule, for instance, inferred the existence of three propyl alcohols on the basis of the hypothesis of difference in units of affinity. Kolbe postulated the existence of two isomers of methylpropyl ketone.

As early as 1862 Butlerov abandoned the hypothesis of difference of units of affinity in polyvalent atoms due to his pupil's views on the reciprocal influence of atoms in a molecule.

Butlerov wrote: "Not only here and now, when speaking of the difference of units of affinity, must we draw attention to the factor (see paper on chemical structure) which influences the nature of the units of affinity, of the nature of bonds which link other units; and it is even necessary to add that the difference may be conditioned by this influence" [36].

Concerning the views of Erlenmeyer on the difference of units of affinity, Markovnikov wrote to Butlerov:

"For the present he has abandoned the difference of units of affinity, but once he said to me: 'Wait a bit! I am now keeping quiet about this, but I am working and wish to demonstrate facts. Kolbe is doing likewise.' I answered that then I would be the first to admit the inadequacy of the theory of chemical structure but at the same time I perhaps could not accept the difference of affinity because other causes may also come into play" [37].

The controversies of Markovnikov with Erlenmeyer gradually extended over the most fundamental problems of chemical structure. Markovnikov comments at length on these debates in a letter to Butlerov from Heidelberg on April 12, 1866:

"Disputes arose apropos of the "doctrine of constitution" with which Erlenmeyer concluded his lectures.. After Kolbe had spoken, he reminded us of his communication on the isomerism of glycols which I had not yet read and therefore did not know about the errors which it contained. But in the evening Eremeich (this was what Russian chemists in Germany called Erlenmeyer – author) told me how some chemists had reproached him for publishing your "Prognoses" in his journal; whereupon I asked him why nobody made any comment when he published Kolbe's "Prognoses".

"...I told you that recently we conversed about chemists and your achievments; he then made nearly the same comment as Heinz (in Annalen) and added that they would be far more appreciated if you would completely abandon type formulas. About such type formulas, as you know very well, Butlerov uses brackets and other type attributes not in the sense of types. I know that, but others do not understand this distinction and therefore obstinately cling to types under the impression that they express the same thing. Tell Butlerov that with these people it is necessary to pull out the tongue and smear it with porridge and not to let go, otherwise everything runs off, but to push it again into the mouth. Only then are they able to swallow.

"And after this he says at the lecture that you make use of type formulas!" [38].

In Berlin Markovnikov became acquainted with the trend of the scientific investigations of Adolf Baeyer and his laboratory. He was specially interested in Baeyer's work on the structure and synthesis of indigo and in his method of distillation with zinc dust [39].

During Markovnikov's stay in Herman Kolbe's laboratory there was continuous discussion about problems of the theory of chemical structure. Kolbe did not appreciate that a molecule is qualitatively a specific entity and that was why he could not find a solution of the problem of its internal structure. That was why he sharply criticized the ideas about the bond of atoms in a molecule – ideas first put forward by Lomonosov. As early as 1738-1741 M. V. Lomonosov, in developing his ideas about the linking of atoms, arrived at the conclusion that molecules with differing properties may be obtained by different linkings of the same atoms [40]. Lomonosov's atomic-molecular doctrine of the possibility of formation of molecules by linking of identical atoms was disputed more than 60 years later by Dalton who was of the opinion that "complex" atoms can be obtained only by linking of different atoms. Naturally, it is impossible to credit Kekule with the priority for the idea of the linking of identical atoms, an idea enunciated by Kekule 119 years after Lomonosov.

By rejecting the principle of the linking of atoms in a molecule, Kolbe rejected the main scientific principle of the theory of structure of organic compounds.

Vladimir Vasilyevich makes the following comments about Kolbe's theoretical views:

"Kolbe is remarkably obstinate in retaining his previous views and evidently considered it entirely superfluous to read any criticisms of himself. As a worker in his laboratory my own position was somewhat delicate during these debates. But the logic of events was on my side. The erroneous conclusions of Kolbe largely stemmed from the fact that in his formulas he made use of the old atomic weight of oxygen, and no matter how much I urged him to try to express his ideas with the double bond of oxygen, he refused, believing that it was all the same. Kolbe certainly attached little importance to my objections and obstinately held to his views in face of the facts...When the professor went off, the more daring of his assistants ventured to say that he is wrong. This was flattering to my young self-esteem but I could not help feeling that I owed my victory to my Kazan teacher, and to this I drew the attention of my German comrades" [41].

The most important stage in the development of the theory of chemical structure and in the solution of the problem of isomerism was Butlerov's classic paper on the "Various methods of clarifying some cases of isomerism" which was published in 1863. The author naturally wished to bring the paper to the attention of prominent foreign chemists, in particular Kolbe. Markovnikov wrote, however, to Butlerov:

"He (Kolbe – author) is terribly obstinate and nothing at all will convince him that some of his ideas not only lack all factual basis but are even opposed to the facts. For example, the different methyls in ethane. Due to this I am trying to avoid any arguments on this topic" [42].

In his polemic with Kolbe on the fundamental problems of theoretical chemistry, Markovnikov discussed only the essential problems of science, strictly keeping to facts, just as he expected others to do. He did not agree with Butlerov in his unprovoked attacks on Kolbe, nor with the character of the criticism of A.M. Popov, whose investigations of the oxidation of ketones had proved the fallacy of Kolbe's ideas on isomerism.

In a letter from Heidelberg dated April 12, 1866, Markovnikov frankly states his opinion to Butlerov:

"I now wish to refer to your paper in the Bulletin and, in particular, to the paper by Popov which you certainly wrote. Frankly I must say that I was not pleased with your attacks on Kolbe, because you will thus put a weapon in Kekule's hands; also Popov's paper was too sharp. Such a tone is out of place for a young chemist in relation to a person deserving, in spite of all his mistakes, full respect: it is particularly out of place in relation to Kolbe who would never permit himself to treat anybody so high-handedly as Kekule does. I hope you will excuse me for the strictness of my statement because I do this in the interests of the Kazan laboratory and, consequently, in your own interests. I even think that for the time you should refrain from polemics and stand on the facts" [43].

Markovnikov urgently advised Butlerov to visit Germany for the Naturalists' Congress in order to acquaint a wide circle of German chemists with new researches on the theory of chemical structure. In 1867 the physico-mathematical faculty of Kazan University proposed that Butlerov should go abroad in order "to give Mr. Butlerov the opportunity of personally explaining to foreign chemists his claim to have taken the main part in the development of the trend now being followed by chemistry" [44].

Apropos of this, Markovnikov wrote as follows from Heidelberg to Butlerov in Kazan:

"I congratulate you on your leave of absence and hope to meet you in Leipzig. You must come to Germany in July if you wish to find the professors at their work, because in August everybody goes away to various places. Yesterday Kolbe told me that he would be very pleased to meet you but he will be staying in Leipzig only until the beginning of August. Nothing has yet been heard about the Naturalists' Congress and possibly there will be no congress at all this year" [45].

In 1864 Butlerov summarized his investigations on the creation of the theoretical bases of organic chemistry and published a substantial work on "Introduction tothe Complete Study of Organic Chemistry". This classic book was the first in the history of world chemistry in which the theory of structure permeated the whole of organic chemistry. Markovnikov made these noteworthy comments about Butlerov's book:

"We certainly cannot help feeling proud that a work has been published in the Russian language which for the first time presents a detailed exposition of a doctrine which over a period of a quarter of a century has continued to render such dazzling services to science. We must be particularly grateful to A.M. Butlerov because, knowing what a limited circle of readers there is for his book in Russia, he did not follow the example of many Russian scientists by first publishing important work in foreign languages" [46].

However Markovnikov conscientiously examined the work of his teacher in the original and made a number of critical comments in regard to some chapters and sections.

With his inherent scientific conscientiousness and the bluntness of the Russian, he told Butlerov what he thought about the "Introduction":

"I have read a part of the "Introduction" and it seemed to me that some of the sections were too compressed, for example the historical outline of the theory; so that to anyone wishing to familiarize himself with this aspect of the history of chemistry it would be impossible to keep it in mind from your outline unless he nearly learned it by heart" [47].

Markovnikov advised Butlerov:

"...It would be desirable for a part of the theoretical considerations on the existence of different new substances to be replaced by a more detailed enumeration of the compounds in this group and their diverse transformations...It also seems to me that the inclusion of amino acids and certain others in the section on nitrogen-containing compounds, although in accordance with your adopted classification, is inconsistent with their natural connection with the halogen and hydroxy acids" [48].

In defending the interests of Russian science, Markovnikov fought energetically to establish the priority of A.M. Butlerov in the creation of the theory of chemical structure not only by word but with the pen. One of the elements of this struggle was his resolute participation in the translation of Butlerov's "Introduction" into German. Vladimir Vasilyevich considered it necessary to warn his teacher:

"Your hopes for help from Beilstein and Erlenmeyer are likely to be disappointed. Each of them is busy with his own work and the second in particular has little free time. He is bringing out a handbook of organic chemistry" [49].

In 1867 the German edition of "Introduction to the complete study of organic chemistry" was published in Leipzig under the closest participation of Markovnikov. This gave foreign chemists the opportunity of becoming well acquainted with Butlerov's theory of chemical structure as applied to all classes and groups of organic compounds.

Markovnikov wrote: "In the interests of science and my teacher, I cannot fail to rejoice at the appearance of this translation. Having lived two years in Germany and become acquainted with many chemists, I am convinced that such a publication was needed".

In the pages of his magisteral dissertation on the "Isomerism of organic compounds", Markovnikov demonstrated for the first time the utter inadmissibility of Kekule's pretensions to priority in the creation of the theory of chemical structure which were afterwards echoed by some foreign chemists. In this work Markovnikov wrote:

"While being an ardent supporter of the theory of types, Kekule has recently become an adherent of the same theory which was developed in detail by Butlerov under the name of chemical structure. But unfortunately we do not find that acknowledgment of priority which was rightly to be expected from Kekule; it appears that the idea itself is still not sufficiently clearly appreciated". [27].

In his researches Kekule did indeed adhere strictly to the theory of types. While putting forward the concepts of valence of elements, of the linking of atoms and of the chemical constitution of compounds, Kekule simultaneously expressed his belief in the conditionality, subjectivity and arbitrariness of the concepts of atoms, molecules and structure (constitution) of chemical compounds. Generalizing the experimental material which did not fit into the framework of Gerrard's theory of types, Kekule began to develop the concepts of mixed and complex types. Following Gerrard, Kekule asserted that "rational" formulas describe only the chemical transformations of a substance and are incapable of reflecting its internal structure.

Markovnikov emphasizes that: "The importance which Kekule attaches to types is already evident from the fact that each rational formula in his papers is accompanied by the corresponding type. This desire to permanently class all substances in specific types compels him to attribute to them more significance than they actually deserve and to thereby relegate valence to a secondary place" [27].

In making a systematic analysis of the theoretical studies of Kekule and in particular of his textbook of organic chemistry, Vladimir Vasilyevich remarks:

"His rational formulas are nothing else than transformation formulas (Umsetzungsformeln) and not constitutional formulas. That is why he often thinks several formulas can be given for one substance, these formulas serving to indicate different analogies..." Markovnikov makes this final comment at the end of his critical survey: "The student reaches a faulty conclusion if, relying on the word of Kekule, he considers the latter to be the founder of the modern theory of constitution" [27].

In defending the priority of A.M. Butlerov, Markovnikov considered it necessary to publish a paper on the "History of the doctrine of chemical structure" also in a German journal [51]. In this paper, operating with facts, he demolished all attempts by Kekule to rob Butlerov of the credit for founding and developing the theory of chemical structure. This paper had a great effect on foreign chemists. It had a hostile reception among the supporters of Kekule who, in the absence of any factual data and scientific arguments in support of Kekule's priority, were unable to reply to it in print. However, on meeting Markovnikov they expressed their displeasure because of the publication of his paper. Apropos of this Markovnikov wrote as follows from Heidelberg to Butlerov:

"Concerning my paper about Kekule, there were no other unpleasantnesses apart from those about which I wrote to you. But even these were enough. It is difficult to prove that I said nearly the same in my dissertation because they are unable to read it. I told this to Erlenmeyer and he himself said that Baeyer believed on the contrary that you had written the paper" [52].

At the first meeting of Markovnikov with Baeyer an argument ensued about Markovnikov's paper on the "History of the doctrine of chemical structure". Markovnikov gave a full account of this argument:

"We argued the very first time. Baeyer asked whether I had really written the criticism of Kekule's book and when I answered in the affirmative I decided to go into battle. He reproached me with attacking Kekule as if he were a highwayman and toward the end I said: 'I wish you would also analyze Kekule's book, then you would see that nothing would remain of it' " [53].

Markovnikov informed Butlerov that Frankland in his papers ignored the theory of chemical structure and spoke only of the preparation by Butlerov of trimethylcarbinol [54].

Markovnikov wrote: "It is noteworthy that Frankland appears deliberately to be ignoring my work in all his papers. This is certainly because I am one of your pupils" [55].

And for many years afterwards Markovnikov continued to assert the indisputability of Butlerov's priority. In his inaugural lectures at the Novorossiysk University he declared:

"In speaking of the development of the theory of chemical structure, I pointed out that Kekule at first did not participate in its foundation. Soon, however, he published his well-known theory of aromatic compounds. In broad outline he did not put forward anything more than the application of the principles of chemical structure to the group of so-called aromatic substances, substances which are characterized by some fairly conspicuous features" [56].

The historical role of Butlerov in the founding and development of the theory of chemical structure was revealed, after Markovnikov, by D.I. Mendeleev [57] and by the most outstanding Russian chemists — S.V. Lebedev and others [58].

In his introductory lecture to the course on "Development and modern status of the doctrine of valence", delivered in Petersburg University on October 28, 1913, the celebrated Russian chemist S.V. Lebedev said:

"The fruit of the recognition of the quadrivalence of carbon, as I have already indicated, was the founding of the structural theory. The organic development of this theory is to the immortal credit of A.M. Butlerov" [59].

A vivid description of the scientific value of Butlerov's theory of chemical structure in the development of organic chemistry was given by A.E. Arbuzov in his address at the 5th Mendeleev Congress at Kazan in 1928. A high place was accorded to A.M. Butlerov, on the score of his creation of the theoretical bases of modern organic chemistry, in papers by A.I. Gorbov [60] and S.N. Danilov [61] published long before the historical surveys of recent years.

Russian chemists worthily continued the scientific-patriotic initiative of V.V. Markovnikov in asserting the priority of the great founder of the theory of chemical structure and, like Markovnikov, have creatively elaborated and enriched his notable scientific heritage.

In the thirties of the 19th century Dumas and Laurent detected the presence in organic compounds of "hydrogens" of diverse chemical natures — "metallic" and "metaleptic" hydrogens.

In the fifties of the 19th century N.N. Beketov proposed the principle of the "chemical value" of elements [62]. Beketov's principle showed that one and the same element has a different "chemical value" in different compounds due to the influence on it of other atoms or other groups of atoms present in these compounds.

Beketov wrote: "The carbon linked with hydrogen imparts to it quite a different chemical value (preferentially metaleptic) than the value it has in compounds with halogens in which it plays the part of a metal" [63].

Beketov's observation of the dependence of the chemical nature of an element on the chemical nature of the other elements present in a compound was the first step toward the understanding of the properties and reactions of inorganic and organic substances.

Logically following on Beketov's researches were the investigations of N.N. Sokolov on the question of the functional difference of atoms of hydrogen in chemical compounds. In studying the properties of lactic acid and of glycolic and glyceric acids (which he synthesized), Sokolov showed that hydroxy acids contain hydrogen atoms of diverse chemical natures — acidic and alcoholic. On the basis of his observations, Sokolov differentiated clearly between the concepts of basicity and valence of organic compounds. According to Sokolov, organic compounds contain all degrees of transition from metallic to metaleptic hydrogen [64]. In the light of Sokolov's ideas, the difference in character of hydrogen atoms is governed by their position in the molecule, the difference being intensified with increasing distance from one another in the carbon chain, when the influence of the atoms falls.

"This difference, although completely specific, is not sharply defined between two atoms but is intensified with increasing distance of the members from one another; finally it becomes completely definite" [65].

N.N. Sokolov correlated the diverse chemical properties of hydrogen in organic compounds with the amount of caloric contained in them; this was the prototype of the contemporary doctrine of the store of energy of atoms. The views of N.N. Sokolov, generalized by much experimental material of organic chemistry, played an important role in the foundation of some premises for the doctrine of the mutual influence of atoms in a molecule, although

they were limited by the framework of the unitary theory.

A.M. Butlerov highly valued the work of N.N. Beketov in theoretical chemistry. In proposing Beketov as corresponding member of the Academy of Sciences in 1877, Butlerov said:

"The principal studies and papers of Professor Beketov are distinguished by the outstanding feature that they concern the fundamental general problems of chemistry and consequently those whose solution is particularly important for the successful development of science. His very first paper, published in 1854 in the Bulletin of the Academy, related to "linked compounds and linking formulas" and thus concerned one such problem of organic chemistry" [66].

Even earlier Butlerov put a high valuation on the researches of N.N. Sokolov [67].

Beketov's ideas on the "chemical value" of elements and the views of Sokolov on the varying chemical nature of hydrogen in organic compounds were generalized, critically modified on the basis of the principles of chemical structure and raised to a higher level by A.M. Butlerov.

Butlerov's theory of chemical structure was the first to establish the existence of a definite order of bonds of atoms in a molecule, the direct and indirect bonds of atoms. It showed that the qualitative distinguishing feature of each molecule is determined not only by its composition but also by the order of the chemical bond of its atoms.

Butlerov declared: "The properties of a substance clearly indicate that each element exerts a specific influence upon the chemical content of the elements combined with it, and, conversely, is subject to the influence of the latter" [68].

Butlerov's theory was not restricted to the recognition of the chemical structure of molecules, the chemical interaction of atoms directly linked to one another. Butlerov's theory also indicated the occurrence in molecules of chemical interaction of atoms of another category – the reciprocal influence of atoms not directly linked together. Butlerov's structural formulas expressed the main, direct bonds and the principal chemical interactions of atoms in a molecule, characterizing the basic features of its chemical structure and chemical behavior. The problem posed by Butlerov about the indirect linkages in molecules governed the further development of the theory of chemical structure.

The main credit for the discovery of the laws of intramolecular mutual influence of atoms, for the founding and development of the doctrine of the mutual influence of atoms, belongs to V.V. Markovnikov. At the very start of his scientific activity, Markovnikov applied the principle of mutual influence of atoms to the study of the isomerism of allyl alcohol and its bromides, and also to the isomerism of oxygen-containing derivatives of propane [69].

The value of these investigations of Markovnikov for the establishment of the theory of chemical structure was noted by Butlerov in a specially written article [70].

In his magisteral dissertation (1865) Markovnikov quite clearly and definitely put forward the problem of the study of the reci procal influence of atoms in chemical compounds as a chemical problem of the first importance.

He wrote: "The time has not yet arrived when we can accurately determine the degree of influence exerted by a given atomic grouping on all the chemical and physical properties of compounds".

"...Until we know all the internal and external conditions causing a substance to undergo metamorphosis, until we can determine what amount of chemical energy a given element contributes to the total amount of action, a knowledge of the true constitut ion will be impossible" [27].

With the objective of clarifying the various phenomena of reciprocal influence of atoms within a molecule, Markovnikov persistently and continuously studied numerous represenatives of the principal classes and gro ups of organic compounds and gradually accumulated experimental material obtained in a great variety of physical and chemical conditions.

Systematic investigations in this direction were undertaken in Markovnikov's laboratory under his guidance:

"Krivaksin will oxidize amylene chlorohydrin to obtain $ClH_2CCOC_3H_7$ or chlorovaleric acid, according to the mode of addition of the hypochlorous acid. Aleksandrysky will prepare isomeric dichloroacetone from dichlorohydrin. Sorokin is already studying the mode of arrangement of chlorine and iodine on their addition to unsymmetrical unsaturated hydrocarbons...In my opinion, only by such systematic work can we ever arrive, for some conditions at least, at an understanding of the influence of atoms and of their relative energy in reactions" [71].

Also in Germany the ideas of the mutual influence of atoms governed all his experimental investigations. From Leipzig Vladimir Vasilyevich wrote to Butlerov:

"I am sending my paper on acetonic acid to Annalen strictly because this is a good opportunity of enunciating some considerations about the mutual influence of elements in compounds on their chemical character. I again had to attack Kekule a little for the view he expressed about the order of substitution of hydrogen by chlorine in benzene. The paper has been lying with Kolbe for more than a week; he was going to correct it in respect of the language and always says "sometimes". By the way, I must tell you that I have now succeeded in convincing him of the impossibility of existence of two glycolic acids" [72].

In the forword to his doctoral dissertation on "Material for the problem of the mutual influence of atoms in chemical compounds" (1869) Markovnikov particularly stressed the indissoluble connection between the doctrine of mutual influence of atoms and the theory of chemical structure. He showed that the study of the interconnections and interdependences of the components of molecules broadens and deepens our knowledge of the chemical structure of organic compounds.

"The problem of the influence of atoms on the direction of chemical reactions of a compound is among the most exciting questions of modern chemistry and, as already noted, it is more and more holding the attention of chemists. It had naturally to arise as soon as the doctrine of chemical structure had been adopted by the majority, and it is a direct continuation and further development of this doctrine" [73].

V.V. Markovnikov defined mutual influence as the qualitative change of properties of one and the same atom in different chemical compounds: "The character of each component atom of a molecule is governed by the properties of the element with which it entered into combination, and vice versa" [73].

In studying the diverse changes of the chemical nature of atoms brought about under the influence of other atoms combined with them, Markovnikov discovered the chemical law: "The character of elements in compounds is governed not only by the elements directly linked to them but also by those which are associated with them in a chemical system through some other polyatomic element" [73].

The researches of Markovnikov established that the character and degree of reciprocal influence of not directly linked atoms depends on their position in the molecule, on the chemical nature of the surrounding atoms and on the distance separating them.

Markovnikov wrote: "In general the influence of any given element on another is weakened with increasing separation distance in the total chain of chemical action containing all the elements in the molecule" [73]. "...Hence (he concludes) in addition to qualitative and quantitative influences we have the influence of difference of arrangement..." [73].

On the basis of these general laws, Markovnikov conducted systematic investigations on the manifestation of the influence of each individual atom and each individual group of atoms on the chemical nature of the remaining atoms in a molecule. By this method Markovnikov established the theoretical rules for reactions of substitution, scission and addition which are known as the Markovnikov rules.

Subsequently Markovnikov revealed the connection between the reciprocal influence of atoms and the conditions of the external medium which was a decisive step in the study of the directions and methods of study of chemical reaction.

In 1876 he formulated a general rule for reactions of addition to unsaturated molecules: "If an unsaturated molecule CmHnX combines with a saturated molecule YZ, at a relatively low temperature the negative element or group joins on to the least hydrogenated carbon or to the carbon already joined to the negative element (group), while at a higher temperature the addition takes place in the converse order" [74].

Markovnikov's work in the field of the reciprocal influence of atoms revealed to research workers entirely new methods in the study of molecules.

The theoretical rules of Markovnikov were guiding principles in the determination of the fine structure of organic substances, in the study of their reactions and most important transformations in nature and technology. They played an outstanding part in the development of the theory and practice of organic synthesis.

The notable investigations of Markovnikov's pupil, M.I. Konovalov, on the action of nitric acid on paraffinic hydrocarbons gave exhaustive proofs of the correctness of Markovnikov's rules for substitution in saturated hydrocarbons [75].

The doctrine of the reciprocal influence of atoms was born in the fight with metaphysical and mechanistic concepts in chemistry which regarded the molecule as a simple mechanical collection of atoms. Prominent

representatives of Western European chemistry such as Kolbe, Erlenmeyer, Kekule, V. Meyer, Graebe, reduced the molecule to the sum of its component parts, denying the chemical interactions and interconnections of the components even as a whole in the molecule. In opposition to the principle of the reciprocal influence of atoms they supported the principle of additivity in chemistry. Applying this principle to problems of structure, they reduced the molecule to a simple mechanical chain of individual atoms, while they reduced the qualitative differences between atoms in molecules to purely quantitative differences.

Graebe (a well-known pupil of A. Baeyer) thus asked Markovnikov:

"Why does the chlorine in acetyl chloride differ so markedly from chlorine in ethyl chloride ?"

Markovnikov wrote: "I cannot fail to remember this, nor the numerous and prolonged debates which I had with Kolbe... Already in the first year of my stay in Germany I was convinced that the Kazan laboratory was theoretically a long way ahead of all the German laboratories" [76].

As V.V. Markovnikov indicates, his concepts confirmed the qualitative differences between identical atoms in different molecules; "the laws derived therefrom, confirmed by many important reactions, were then completely novel or even conflicted with extremely authoritative concepts (of Kekule)" [77].

The metaphysical conception of the world of West European chemists — supporters of the idealistic philosophy of Kant — prevented them from understanding the doctrine of the reciprocal influence of atoms which raised to a new qualitative level our knowledge of the structure of organic and inorganic substances and enabled a deeper penetration into the interior of their molecules.

The scientist-materialist V.V. Markovnikov regarded the molecule as a self-balanced dynamic system of interacting atoms. He states that "the existence of molecules with properties known at a given instant is the result of the mutual influence of its atoms. In specified conditions these influences must be identically balanced, otherwise we should not be able to conceive why, in identical conditions, a molecule always has the same properties. The study of these conditions is one of the main problems of chemistry" [78].

The intramolecular reciprocal influence of atoms and the stability of molecules are indissolubly linked, in Markovnikov's opinion, with the external conditions (temperature).

From his studies of molecular dynamics and the interaction of the component parts of molecules, Markovnikov established that chemism is motion. He regarded the chemical form of motion as a special type of motion, a qualitatively different form of motion: "Just as heat and light are manifestations of a known form of motion of material particles, so is chemism also motion. The difference may perhaps reside merely in...the type of motion" [79].

Developing a materialistic trend in chemistry, V.V. Markovnikov is compelled to reject the notions of absolute peace in nature, of the immobility and immutability of chemical compounds.

As early as 1872 he posed the question of the physical — spatial — arrangement of atoms in molecules. In his inaugural lecture at Novorossiysk University Markovnikov says: "It is difficult, however, to conceive that there are not direct and specific relations between the chemical interaction and the physical position of the atoms in a molecule. There are certainly some facts which very strongly support the idea of the existence of such relationships" [79].

The doctrine of the mutual influence of atoms enabled Markovnikov also to be the first to correctly illuminate the problem of free radicals. In his report of 1902 he pointed out: "All the chemical properties of $(C_6H_5)_3C-C(C_6H_5)_3$ are easily accounted for on the assumption that the fourth unit of affinity of the C requires, for satisfaction of its chemical avidity, another affinity than that which may be available to it from the C linked with the three C_6H_5's. Hence the bond between the carbons in R_3C-CR_3 will be easily ruptured, allowing formation of derivatives of the $(C_6H_5)_3C$ radical which are capable of existing. We may here expect different syntheses provided the fourth C unit is satisfied by the appropriate affinity" [80].

In those days foreign chemists, headed by Gomberg, considered hexaphenylethane to be an extremely stable compound, and the views of Markovnikov on the dissociation of hexaphenylethane into two free radicals were in sharp conflict with the generally accepted point of view. Markovnikov's ideas about the structure of hexaphenylethane were experimentally confirmed and developed by his pupil A.E. Chichibabin [81].

In 1904 Chibibabin began his investigations of the structure of triphenylmethyl.

He writes: "The idea of quadrivalence or at least of uneven valence of carbon was firmly fixed in the minds of the overwhelming majority of organic chemists in the whole of the preceding dazzling period of development of organic chemistry. I therefore embarked on the investigation, being deeply certain of the inaccuracy of

Gomberg's explanation of the structure of the hydrocarbon. At the same time I doubted somewhat whether without any assistance I could actually demonstrate beyond all question the error of Gomberg and find the true explanation of the phenomenon discovered by Gomberg.

"The first of my tasks was to show the validity of that formula for triphenylmethyl with quadrivalent carbon which seemed to me to be particularly probable, i. e. the formula of hexaphenylethane. This task was carried out with full success.

"The second problem was to find phenomena, similar to the striking phenomena discovered by Gomberg for triphenylmethyl, among other substances possessing an undisputed structure. This problem, too, was solved in my opinion by the investigation and discovery of some striking properties of pentaphenylethane" [82].

The outstanding value of the investigation of A. E. Chichibabin in the discovery of free radicals and in the detection of trivalent carbon was mentioned by S. V. Lebedev at the inaugural lecture at Petersburg University (1913):

" At this moment, thanks to the efforts of Gomberg, Chichibabin, Schlenk and others, the problem has gone beyond the bounds of any doubts—trivalent carbon exists" [83].

The development of electronic concepts in organic chemistry led to widening and deepening of the laws of intramolecular reciprocal influence of atoms discovered by Markovnikov, to the discovery of the nature of the chemical bonds in various classes of organic compounds.

The ideas and researches of V. V. Markovnikov live on and go on developing in our day, for they are a powerful aid and driving force for the solution of fundamental chemical problems.

The name of Vladimir Vasilyevich Markovnikov can with full justification be grouped in the history of science side by side with the names of A. M. Butlerov and D. I. Mendeleev.

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MECHANISM OF HYDROGEN EXCHANGE AND OF SOME PROTOLYTIC REACTIONS IN SOLUTIONS

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In a previous paper [1] general considerations were put forward about the modes of isotopic exchange of hydrogen in solutions. They can now be corroborated and developed in more detail as a result of investigations which were subsequently undertaken. The problem of the mechanism of hydrogen exchange is of general interest since it is associated with the important problem of the mechanism of many hydrogen transfer reactions and in particular with protolytic reactions in solutions.

I. Rapid and Slow Exchange

Depending upon their ability to undergo hydrogen exchange in solutions, numerous investigated compounds [2, 3] form two sharply differentiated groups. In the first of these the exchange proceeds substantially instantaneously at any given temperature without need for a catalyst. This is true of the N–H, O–H, S–H, Cl–H bonds and many others, although not of all compounds with acid-base donors of deuterium, for example, with D_2O, C_2H_5OD. We propose to call this the rapid type of exchange. In the second group of compounds, exchange either does not take place at all or it only proceeds more or less slowly. The possibility of its occurrence and its velocity are determined by the structure of the molecules and by the nature of the substituents present, by the reaction of the medium and by the properties of the deuterium donor. Exchange of this type (which we call slow) exhibits a strong dependence upon the temperature and upon the presence of catalysts for protolytic reactions. The slow type of exchange is characteristic of the C–H bonds in organic compounds. From the table we see that the type of exchange is not governed either by the properties of the individual bonds in which the exchange proceeds or by the nature of the atom with which the exchanging atom of hydrogen is directly linked. In particular, contrary to the prevalent conception, it is not characterized by the energy, by the polarization, or by the "ionic quota" of the bond.

TABLE

Bond	Bond energy	Length of bond	Dipole moment	Atomic refraction	Constant of bond strength $f \cdot 10^{-3}$	Difference of electronegative activity
N–H	83.7	1.01	1.31	3.42	7.1	0.98
C–H	87.3	1.09	0.4	3.52	5.1	0.52
S–H	87.5	1.35	1.03	8.79	4.0	0.41
Cl–H	102.7	1.28	0.68	7.07	5.1	0.98
H–H	103.4	0.74	0	2.20	5.1	0
O–H	110.2	0.97	1.51	2.63	7.5	1.33

Rapid or slow exchange in the bond of X–H is determined by the presence or absence of free (unsaturated) electronic pairs round the atom X. If these are present, then a deuteron (or proton) may add on to one of them with simultaneous detachment of a proton from the electron pair linked with the other. This process, whose mechanism is considered in detail below, can be represented by the following scheme for, for example, exchange between H_2S and D_2O:

$$D^+ + :\underset{\textstyle H}{\overset{\cdot\cdot}{\underset{\cdot\cdot}{S}}}:H = D:\underset{\textstyle H}{\overset{\cdot\cdot}{\underset{\cdot\cdot}{S}}}: + H^+ \qquad (1)$$

It takes place in a single elementary act and evidently does not require an appreciable activation energy. Hence the exchange takes place very quickly even at low temperature. In the absence of a free

electron pair, as for example in the C−H bonds of organic compounds, the deuteron can only add on at the same electron pair to which the proton is bound, after elimination of the latter. This process demands a considerable activation energy and exchange proceeds either slowly or not at all, depending upon the factors determining the strength of the C−H bond and its ability to release a proton. Various mechanisms possible for this process are considered below.

With the objective of confirming these ideas, several fresh examples of hydrogen exchange were studied in our laboratory. In the Si−H bonds of organosilicon compounds, there are no free electron pairs round the silicon atom and no hydrogen Exchange is manifested in them. In a paper by Khaskin and the author [4] the absence was shown of exchange in triethyl-, triphenyl- and triethoxysilanes $(C_2H_5)_3SiH$, $(C_6H_5)_3SiH$ and $(C_2H_5O)_3SiH$ with D_2O, C_2H_5OD and $(CH_3)_2ND$ even on prolonged heating above 100 deg. This result could not have been predicted on the basis of analogy with exchange in the corresponding tertiary carbon compounds since the Si−H and C−H bonds differ very markedly not only in strength but also in the sign of polarization [5]. In ammonia, various amines and amides [6], possessing a free electron pair round the nitrogen atom, indications of slow exchange were not detected in a single instance, whereas in the ammonium ion the exchange has a measurable kinetics and takes place in the process of hydrolysis with participation of ammonia. This is confirmed by the dependence, found by Sulima and the author [7], of the exchange velocity in ammonium salts on the presence of concentrated strong acids which suppress hydrolysis. This mechanism occurs in slow exchange in the Co: NH_3, Pt: NH_3 and Pd : NH_3 bond of the series of hexammino- and tetrammino- salts whose kinetics depend largely on the pH of the solution [3] *. Hypophosphorous and phosphorous acids have the well-authenticated structure of $O{=}PH_2(OH)$ and $O{=}PH(OH)_2$ corresponding to the absence of a free electron pair round the phosphorus atom. In harmony with this, Sulima and the author [9] found that exchange with D_2O does not occur in the P−H bond of phosphorous acid and its anion and only proceeds very slowly in hypophosphites at 100 deg. In hypophosphorous acid, however, it proceeds in the P−H bond even at 25° with a half-period of 16 minutes. It is impossible on the basis of only the reciprocal influence of atoms to explain these large differences in the exchange susceptibility in such similarly constituted substances. Exchange in hyposphosphorous acid is associated with its tautomeric transformation into the $HP(OH)_2$ form, as is confirmed by a comparison of its exchange and oxidation kinetics. **

According to some literature date [3] gaseous H_2 does not exchange hydrogen for the deuterium of heavy water in the absence of catalysts promoting cleavage of the H: H molecule. Exchange also does not occur in the B−H bonds of borohydrides not possessing a free electron pair round the boron atom; nor is there exchange between BH_4^- and D_2O [13] and between $B_2H_6 \cdot ND_3$ and liquid ND_3 [3].

The now known cases of slow hydrogen exchange are limited to the examples considered and to numerous examples of exchange in the C−H bonds of diverse organic compounds. They are all characterized by the absence of free electron pairs round the atom with which the exchanging hydrogen atom is linked. On the other hand, not a single case is known*** where exchange would proceed very quickly if such pairs were present. We can therefore claim that the considerations here discussed are sufficiently well founded.

II Mechanism of Rapid Exchange

Rapid exchange of hydrogen between a substance XH (see * on next page) and heavy water (or other deuterium donor with acid-base functions) is usually explained by electrolytic dissociation:

$$XH + D_2O = X^- + HD_2O^+ = XD + HDO, \tag{2}$$

if XH is an acid, or

$$XH + D_2O = DXH^+ + OD^- = XD + HDO, \tag{3}$$

if XH is a base relative to water (or the dissolved catalyst). However, an unmeasurably high velocity of exchange is observed even with extremely weak acids and bases and it is not appreciably slowed down by addition of a large excess of strong acids or bases when the equilibrium concentrations of the products of dissociation of XH fall to 10^{-10} and lower. Such low concentrations of ions cannot lead to rapid exchange.

* Here and later references are made to [2] and [3] as sources of original literature.

** In a study of the reduction of diazonium salts in D_2O Miklukhin and Rekasheva [11] also found slow exchange in the P−H bonds of hypophosphorous acid. In a recent investigation Jenkins and Yost [10] obtained results in agreement with ours for exchange of H_3PO_2 with T_2O. In their paper exchange was also explained by tautomerism, although only on the basis of the above-mentioned comparison of the exchange and oxidation kinetics.

*** Apart from indication [12] of slow exchange between gaseous : PH_3 and liquid D_2O, the kinetics of which is possibly determined by the diffusion of the poorly soluble phosphine in the bulk of the solution.

It is necessary to assume that rapid exchange proceeds independently of the electrolytic dissociation of (2) or (3) (which is not the cause of the rapid type of exchange) and of the simultaneously proceeding parallel reaction (also capable of leading to exchange), and that therefore the velocity of rapid exchange is not directly associated with the strength of the acids and bases taking part in the exchange. According to the considerations here advanced, rapid exchange between substance XH and a deuterium donor YD is effected in a single elementary act through the intermediate state (a) by simultaneous transfer of a proton to the free electron pair of atom Y and of a deuteron to the same pair of atom X:

$$\begin{array}{c} \ddot{X}H + \ddot{Y}D = \begin{array}{ccc} X & \text{—} & H \\ \uparrow & & \downarrow \\ D & \text{—} & Y \end{array} = :XD + :YH \end{array} \qquad (4)$$

(a)

This symmetrical process does not require a high activation energy apart from that expended on a favorable orientation of the exchanging molecules and on equalizing the interatomic distances of X−H and Y−D. The activation energy of anomalous electronegativity, according to Grotthus, possessing a similar mechanism, is only 2-3 kcal/mole as calculated from its temperature coefficient. On the other hand, the symmetrical structure of the intermediate state and the encirclement by molecules of solvent exclude abnormally low values of the exponent. Reactions with these characteristics proceed unmeasurably fast even at low temperature. Exchange according to scheme (1), which differs from (4) by the participation of three molecules in one elementary act, may proceed in a strongly acidic medium with a large excess of hydroxyl ions.

Electrolytic dissociation (2) may be represented, taking account of solvation of ions, by the following exemplary scheme:

$$YD + XH + YD = YD\ldots\overset{-}{X}\ldots\overset{+}{H}\ldots YD = YDX^{-} + HYD^{+}. \qquad (5)$$

Unlike (4) this process requires considerable energy for scission of the X−H bond, which is compensated to a greater or lesser degree by the energy of solvation of the ions. Its activation energy depends both on the properties of the scissionable bond and on the energy of interaction of the solvent of YD with the solvatable ions. These account for the diverse values of the strength of acids and bases in dependence upon their structure and the solvent; they also account for the diverse rates of dissociation which proceeds more slowly, for instance, in C−H bonds. The very low acidity of hydrocarbons is apparently due to the absence of free electron pairs, so that the energy of cleavage of a proton from the C−H bond is not compensated by the simultaneous covalent addition of a molecule of the solvent to the formed carbanion according to scheme (5).

In hydroxyl compounds rapid exchange is likewise not associated with the formation of free hydroxyl ion, while in presence of free electron pairs it proceeds by the same mechanism (4):

$$ROH + YD = \begin{array}{ccc} R-\ddot{O} & \text{—} & H \\ \uparrow & & \downarrow \\ D & \text{—} & \ddot{Y} \end{array} = ROD + YH \qquad (6)$$

For example, in ethyl alcohol an exchange equilibrium is rapidly established with D_2O [14].

Attention has already been drawn by Miklukhin [16] to the role in hydrogen exchange of intermediate complexes formed by hydrogen bonds.

Exchange of water with liquid ND_3, DBr, D_2S, etc. does not introduce any fundamental changes into these schemes. The acidic or basic properties of these solvents, of decisive importance for the slow type of exchange, should not play an important role in the rapid type of exchange.

III Mechanism of Slow Exchange

In the absence of free electron pairs round atom X, exchange may likewise take place by a mechanism formally identical with (4), but with the important difference that a deuteron may only join on covalently to that electron pair which previously bound the proton and only after the removal of the latter has freed the pair.

• Here and later, for the sake of simplicity, the symbols XH and YH used to denote both the exchanging bonds and the exchanging molecules themselves.

This process has a considerably higher activation energy than is the case in the rapid type of exchange. In the intermediate quaternary complex formed by hydrogen bonds, such a proton transition does not occur at all or is greatly slowed down in dependence on the height of its potential barrier. The latter is determined by the structure and arrangement of the electronic densities in the exchanging molecules; it is also influenced by the properties of the medium, whereas these factors have little importance for rapid exchange.

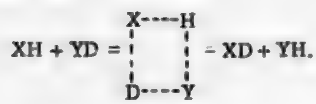
The ratio of the velocities of electrolytic dissociation of (2) or (3) and of the type (4) process determines the mechanism of slow exchange. If electrolytic dissociation is the faster process, then exchange takes place through the stage of formation of free ions according to the scheme:

$$XH + YD = X^- + HYD^+ = XD + YH \qquad (7)$$

in an alkaline medium, or

$$XH + YD = DXH^+ + Y^- = XD + YH \qquad (8)$$

in an acid medium, and other intermediate stages are possibly involved. This is usually referred to as the ionization mechanism. But if a type (4) process proceeds more quickly than electrolytic dissociation, then exchange is accomplished in a single act via the intermediate complex formed with hydrogen bonds and not with covalent bonds:



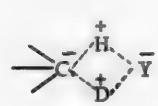
(9)

This is usually known as the association mechanism. Both mechanisms are very common in the C−H bonds of organic compounds, and the rest of this paper will be devoted to their consideration.

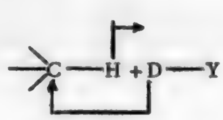
IV. The Association Mechanism

Due to the great electrophilicity of the proton, the association mechanism of hydrogen exchange resolves itself into a mechanism of electrophilic substitution. Systematic study of the exchange with deuteroacids in aromatic compounds has shown that it is facilitated by the same factors which facilitate electrophilic substitution (sulfonation, nitration, halogenation, etc.), namely, high acidity of the deuterium donor and of the substituent which increases the electron density at the carbon atom in the C−H bond in which the exchange is proceeding. For example, Shatenshtein [17] showed that exchange of hydrocarbons with liquid deuterium bromide is accelerated by introducing electropositive substituents, $-CH_3$ and $-OCH_3$, and is slowed down by introducing electronegative substituents, $-CN$ and $-NO_2$.

In typical cases the electrophilic substitution of hydrogen proceeds apparently via the intermediate quaternary complex



but we must also reckon with the possibility of other mechanisms of electrophilic substitution entering into consideration in organic chemistry, for example:



with participation of a third molecule.

Comparison of the rate of exchange of benzene with pure and dilute D_2SO_4 [15] and other date confirm that free hydroxyl ions are not involved in the association mechanism. This markedly differentiates it from the ionization mechanism (8) in an acidic medium. Other differences between both mechanisms will be indicated below.

V. The Ionization Mechanism

The ionization mechanism must be considered typical of slow exchange with basic donors. It is favored by factors which facilitate the first ionization step - basicity of the medium or the presence of basic catalysts and substituents reducing the electronic density at the carbon atom in the exchanging C−H bond. The influence of substituents, as we know, is manifested in a complex manner and cannot by any means always be precisely predicted. We can cite a number of examples, however, in which it is simply correlated with the exchange susceptibility [2, 3]. Methane, ethane and benzene do not exchange hydrogen with water, but in nitromethane, nitroethane, nitroethane and 1,3,5-trinitrobenzene, exchange takes place and is catalyzed by alkalies. The former are capable of rearranging into aci-forms with detachment of a proton from the C−H bond. In presence of alkali, exchange also proceeds in acetamide and acetonitrile. In these examples electrons are attracted by the negative NO_2 CN and CO groups. The enhanced ability of the C−H bond to undergo ionization round the ternary C≡C bond is manifested in the facility of exchange of acetylene with water in presence of alkali. In exchange by the ionization mechanism an extremely important part is played by $\sigma - \pi$ conjugation, whose importance for various organic chemical reaction has been demonstrated by Nesmeyanov [19]. The dependence of exchange of α-hydrogen on the conjugation in the H−C−C=O chain was confirmed by Nesmeyanov, Kursanov and co-workers [20] in cyclic ketones, acetylacetonates and dibenzoylmethane, and later by Shatenshtein [23] in hydrocarbons. Exchange in the methylene group of acetylacetone and ethyl acetate proceeds considerably faster than in acetone due to the participation of two C=O groups linked to the α-carbon in the conjugation. For the same reason exchange proceeds relatively easily in the methylene group of malonic esters and ethyl cyanoacetate, which may be correlated with their known facility of condensation with carbonyl compounds. In acetates the conjugation in two chains − the H−C−C=O chain and the M−O−C=O chain − comes simultaneously into play and, as Mikhulin [22] showed, exchange in their methyl group proceeds with greater facility the lower the polarity of the M−O bond. Conjugation of the C−H bond with the nucleus in the methyl group of toluene is insufficient for exchange in the latter with water, but in our laboratory we found [31] that exchange proceeds in nitrotoluenes and is catalyzed by alkalies, as was to be expected.

Up to recently the study of hydrogen exchange in the liquid phase had been almost entirely restricted to aqueous solutions where the acidic properties of the C−H bond are manifested only to a very minor extent and their differences are largely equalized. Recent papers by Shatenshtein and co-workers [23] deal with the slow hydrogen exchange of many hydrocarbons in liquid ND_3 which is a much stronger base than water. In it, especially in presence of the even stronger base, potassium amide, exchange takes place with greater facility than in water, and its velocity quantitatively characterizes the acidity of the hydrocarbons [24]. The difference between mechanisms (7) and (9) is particularly clearly manifested by the inhibiting effect of substituents on the exchange of hydrocarbons with ND_3 and DBr. All these, as well as a series of other data, confirm the modes of slow hydrogen exchange in solution here discussed.

VI. Steps of the Ionization Mechanism

The ionization mechanism of exchange (8) in an acid medium is typical of carbonyl and certain other compounds capable of adding on a proton to the C=O, C=N, etc. bonds. It differs fundamentally from the associative electrophilic mechanism (9) in that the addition of a proton (or deuteron) and exchange take place at different carbon atoms with migration of the reaction center [19] and in separate steps.* In the first, usually rapid, step a proton is transferred from the acidic solvent or catalyst to the dissolved molecule. In the resultant onium cation the neighboring C−H bond is weakened and this leads to exchange or to other protolytic reactions involving one or more slower steps. This general scheme is confirmed by a series of kinetic studies [3].

There are insufficient well-founded experimental data about the individual intermediate steps of exchange according to the ionization mechanism (7) and in particular (8). Various schemes have been advanced for these and other protolytic reactions; we shall consider only the most typical of these [3, 16, 18, 26]. Their comparison may give a criterion of their reliability.

There is such a great similarity between hydrogen exchange, enolization, racemization and halogenation of ketones in presence of bases that an identical mechanism must be assumed for the first slow step: transition of proton from the C−H bond to the base B:

$$\underset{\displaystyle CH_3}{R-\overset{|}{C}=O} + B = \left[\underset{\displaystyle CH_2}{R-\overset{|}{C}-O}\right]^- + BH^+ \tag{10}$$

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* The difference between mechanisms (8) and (9) roughly corresponds to the difference between a "bimolecular" (S_E2) mechanism and a "monomolecular (S_E1) mechanism (to use the terminology of the English school [18]). This terminology cannot be considered a happy one since a solvent or catalyst usually participates in the reaction and this renders very indeterminate the difference in the molecularity and kinetic order of the slow step.

The reverse reaction (10) with BD^+ leads to exchange, while addition of a proton to the oxygen leads to enolization. The duality of the reaction of the intermediate ion is explained, according to Nesmeyanov [19], by transfer of a reaction center on the conjugated chain from the α-carbon to the carbonyl oxygen under the influence of the reagent, and does not require to be explained by any fundamentally inaccurate or sterile resonance or mesomerism concepts.

This mechanism is confirmed by many experimental facts, but it is unsuitable for oxygen exchange of ketones with H_2O^{18} in presence of alkalies because it evidently does not lead to such an exchange. For the latter it is suggested that the slow step is the addition of hydroxyl to the carbonyl carbon:

$$R-\underset{R}{C}=O + O^{18}H^- = R-\underset{R}{C}\begin{matrix}\nearrow O^- \\ \searrow O^{18}H\end{matrix} \qquad (11)$$

followed by migration of a proton from one oxygen atom to the other and later by addition of a proton (from the alkaline solvent) with formation of a symmetrical orthostructure $R_2C(OH)_2$. In order to get round these difficulties, some authors prefer a mechanism of primary addition of water at the double carbonyl bond:

$$R-\underset{R}{C}=O + H_2O^{18} = R-\underset{R}{C}\begin{matrix}\nearrow OH \\ \searrow O^{18}H\end{matrix} \qquad (12)$$

Such primary steps as (11) or (12) with diverse variants of the succeeding steps are assumed for reactions of hydrolysis of carboxylic esters, oxygen exchange in aldehydes, carboxylic acids and their esters, etc. in presence of bases or in a neutral nedium. In D_2O^{18} however, acetone exchanges both hydrogen and oxygen with commensurate velocities [25]. On the basis of the mechanisms considered, it is necessary to assume that we have simultaneously, and with similar velocities, the reaction (10) of detachment of a proton and reaction (11) or (12) of addition of hydroxyl ion or water. The unsatisfactory character of such a hypothesis indicates the dubiousness of these mechanisms.

Even greater difficulties stand in the way of a detailed knowledge of mechanism (8) of isotopic exchange and other protolytic reactions of carbonyl compounds in presence of acidic catalysts. For the above-mentioned reactions of ketones, the first (rapid) step is considered to be the transfer of a proton from the acid BH to carbonyl oxygen:

$$R-\underset{R}{C}=O + BH = R-\underset{R}{C}-OH^+ + B^- \qquad (13)$$

Addition of a proton to carbonyl weakens the neighboring C—H bond and the proton can transfer from it to water with formation of an enol. Transfer of a proton from the C—H bond to the base remains the slow step if we ignore the cases of a very weak acid BH and molecules with a very strongly polarized C—H bond. This mechanism accounts for enolization but not for exchange, for which it is necessary to assume subsequent steps with participation of the enol. Consequently, in an alkaline medium, hydrogen exchange is regarded as a reaction proceeding in parallel with enolization and independently of it; in acid medium it is considered to proceed via the enolization step. Such a dualism is likewise doubtful.

For the hydrolysis of carboxylic esters in presence of acids after a step analogous to (13), further steps with participation of water are necessary. Various suggestions have been made apropos of the latter and they can be reduced to three fundamental variants [26]: 1) cleavage of alcohol with formation of a $[R-C=O]^+$ ion, ion, followed by addition of water to it; 2) exchange of a proton for an alcohol radical between $\left[R-C\begin{matrix}\nearrow OH \\ \searrow OR\end{matrix}\right]^+$ and water; 3) addition of water to the same ion with formation of the orthoester of the monocarboxylic acid, which then splits off alcohol. Esterification reactions proceed trhough the same steps in the reverse order. Similar schemes explain the oxygen exchange in ketones and carboxylic acids; in this connection, for consistency with kinetic data and the presence of general acid catalysis, we must assume the slow step of transfer of a proton from acid to carbonyl or from the latter to the base conjugated with the acid BH [25]. Both are equally unlikely.

The unsatisfactory nature of all these schemes induced some authors [18, 27] to revert to the old trimolecular mechanism of Lowry, according to whom a proton (or deuteron) is transferred in one elementary act from acid to substrate and from the latter to the base, for example:

$$YD + XH + B = Y + DX + HB. \qquad (14)$$

This mechanism in turn was rejected because the kinetic equations did not contain a term corresponding to it involving the product of three concentrations, but such a conclusion cannot be considered convincing. In particular the trimolecular mechanism of exchange of hydrogen between alkenes and ND_3 was confirmed by

Shatenshtein [23] who found that exchange is accompanied by isomerization with rearrangement of the double bond.

If the deuterium donor YD and the acceptor B are different reaction centers in the same molecule, then mechanism (14) is similar to mechanism (9) for slow exchange.

VII. Exchange in radicals

Reactions in solutions with participation of free radicals are very common, and we may suggest that a radical mechanism is also encountered in reactions of hydrogen exchange of dissolved substances. This problem is intimately associated with the study of the hydrogen bond in free radicals about which very little is yet known.

Kursanov and co-workers [28] found that saturated aliphatic hydrocarbons exchange all the hydrogen atoms with concentrated D_2SO_4, if they contain tertiary carbon, and that exchange does not take place if the latter is absent. They explain this by a chain process with participation of $R_3C^{\cdot}$ radicals or of R_3C^{+} ions, resulting in rearrangement of the chain and rapid exchange of hydrogen with the acid during the period of their brief existence. Such an exchange demands mechanism other than those considered above. If exchange proceeds in the carbonium ion, then the weakening of the C−H bond by the positive charge of the ion is probably insufficient to account for the rapid exchange. But if it proceeds in the radical, then we can explain the mechanism on the basis of the observation, by Fomenko and Sadovinkova [29], of absence of exchange in triphenylmethyl with D_2O or $(CD_3)_2CO$ even after prolonged heating at 100°. Unambiguous data were likewise not obtained for exchange of radicals with D_2O in a study of Kolbe's electrochemical synthesis with the help of deuterium [16].

Until new experimental data are obtained, another question which remains open is that of the role of transfer of radicals or atoms of differing isotopic composition in hydrogen exchange in solutions. Also requiring study is the possibility of participation of hydride anions in the exchange.

SUMMARY

1. A classification of reactions of isotopic exchange in solutions is advanced which is confirmed by experimental data. Such reactions are of the slow or fast type depending upon the presence or absence of free electron pairs round the atom with which the exchanging hydrogen atom is linked.

2. Exchange of the rapid type proceeds independently of the electrolytic dissociation – a process taking place in parallel.

3. The fundamental mechanisms of the slow type of exchange are discussed.

4. The unsatisfactory features of previously advanced mechanisms of protolytic reactions of carbonyl compounds are demonstrated.

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THIOSULFATE COMPLEXES OF MERCURY

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Thiosulfate complexes of mercury were described long ago in the literature. The following compounds were obtained in solidform:

$$5K_2S_2O_3 \cdot 3HgS_2O_3;\ 3K_2S_2O_3 \cdot HgS_2O_3 \cdot 3H_2O;\ 5K_2S_2O_3 \cdot HgS_2O_3 \cdot H_2O\ [1].$$

The process of formation of complexes of divalent mercury with the thiosulfate radical in aqueous solutions has been utilized for potentiometric titration of the thiosulfate ion with mercuric chloride solution [2]. The maximum potential change corresponded to formation of the complex ion $[Hg(S_2O_3)_2]^{2-}$. The existence of these complex anions was confirmed by Kolthoff and Miller by investigation of the polarographic waves obtained during anodic polarization of the dropping mercury electrode in sodium thiosulfate solutions [3]. The anodic wave is appreciably shifted in the direction of the negative potentials, which indicates high stability of the complex formed. The stability of this complex, however, was not studied.

The thiosulfate residue is a strong coordinated substituent, belonging according to Yatsimirsky's classification to the covalent addends [4].

The thiosulfate complexes of many metals are distinguished by high stability. The values of the instability constants are only known for a few complexes, including the complexes of some divalent metals (Cd^{2+}, Zn^{2+}, Pb^{2+}). Cadmium ions form the complexes $[Cd(S_2O_3)_2]^{2-}$ ($K = 5.3 \cdot 10^{-5}$); $[Cd(S_2O_3)_3]^{4-}$ ($K = 1.6 \cdot 10^{-6}$).

The instability constant of the thiosulfate complex of zinc is equal to $5 \cdot 10^{-3}$ [5]. Thiosulfate complexes of lead are characterized by the following values of constants:

$$K_{[Pb(S_2O_3)_2]^{2-}} = 7.4 \cdot 10^{-6};\quad K_{[Pb(S_2O_3)_3]^{4-}} = 4.5 \cdot 10^{-7}\ [6].$$

Grinberg and Yatsimirsky [7] observed that for the covalent type of bond the stability of the complexes formed by ions of subgroups of the periodic system of D.I. Mendeleev increases with the atomic number of the element. Consequently, thiosulfate complexes of mercury must be more stable than the corresponding complexes of cadmium and zinc.

This paper deals with an investigation of the composition and stability of complexes formed with ions of divalent mercury and thiosulfate ions.

EXPERIMENTAL*

Thiosulfate complexes of mercury were studied by the potentiometric method using a Hartmann and Braun potentiometer. A type GZS–47 mirror galvanometer served as the zero instrument.

The indicator electrode was metallic mercury which had been twice distilled in vacuum. The comparison electrode was a saturated calomel electrode with a potential of 0.244 V relative to the normal hydrogen electrode. The siphons for the electrolytic contacts were filled with 3% agar-agar solution in a saturated potassium nitrate solution. The intermediate electrolyte was a saturated potassium nitrate solution. The starting solution of mercury nitrate was prepared by dissolving 2 g vacuum-distilled mercury in 5 ml conc. nitric acid (d 1.2) and was diluted with water to 1 liter. The concentration of divalent mercury ions in the test solutions was 10^{-3} g-ions/l and $2 \cdot 10^{-3}$ g-ions/l.. Sodium thiosulfate solutions were prepared from the chemically pure salt. The titers were determined by the iodometric method (with potassium bichromate). The test solutions were made up by the following procedure: To a measured volume of $Hg(NO_3)_2$ solution (2.5 or 5 ml) was added the equivalent amount of alkali for precipitation of mercuric oxide, which was then dissolved in a definite amount of sodium thiosulfate solution. The resultant solution was made up to the mark in a 25 ml measuring flask.

Measurements of potentials of the mercury electrode in the investigated solutions were carried out in a water thermostat at a temperature of $25 \pm 0.05°$.

Results of potential measurements are set forth in Tables 1 and 2.

* K. M. Skoryskaya participated in the experimental work.

TABLE 1

Potentials of the Mercury Electrode in Solutions of Complex Mercury Thiosulfates at Low Concentrations of Sodium Thiosulfate.
Initial concentration of Hg^{2+} = 10^{-3} g-ions/liter

Molar concentration of $Na_2S_2O_3$	Activity coefficient of $Na_2S_2O_3$ [13]	$-\log a_{S_2O_3^{2-}}$	Potential of mercury electrode $-E_{Hg}$ (in V)
$3.94 \cdot 10^{-3}$	0.77	2.516	0.1749
$5.91 \cdot 10^{-3}$	0.73	2.364	0.1869
$6.69 \cdot 10^{-3}$	0.715	2.320	0.927
$7.88 \cdot 10^{-3}$	0.69	2.262	0.2005
$9.85 \cdot 10^{-3}$	0.67	2.182	0.2090
$1.97 \cdot 10^{-2}$	0.565	1.953	0.2367
$3.94 \cdot 10^{-2}$	0.49	1.714	0.2633

TABLE 2

Potentials of the Mercury Electrode in Solutions of Complex Mercury Thiosulfates with Excess of Sodium Thiosulfate.
$C_{Hg^{2+}} = 2 \cdot 10^{-3}$ g-ions/liter

Molar concentration of $Na_2S_2O_3$	γ [13]	$-\log a_{S_2O_3^{2-}}$	$-E_{Hg}$ (in V)
$3.91 \cdot 10^{-2}$	0.49	1.717	0.2537
$7.82 \cdot 10^{-2}$	0.47	1.435	0.2817
$1.17 \cdot 10^{-1}$	0.45	1.278	0.2980
$1.56 \cdot 10^{-1}$	0.416	1.186	0.3105
$1.95 \cdot 10^{-1}$	0.386	1.122	0.3108
$3.13 \cdot 10^{-1}$	0.338	0.979	0.3334
$3.91 \cdot 10^{-1}$	0.316	0.908	0.3420
$6.26 \cdot 10^{-1}$	0.272	0.769	0.3577

Determination of the Composition and Instability of Complex Ions

The composition of complexes formed in solutions may be determined from the curve of electrode potential against the logarithm of the activity of the complex-forming salt [8].

The curves plotted from the data of Tables 1 and 2 are convex to the abscissas. This indicates the stepwise character of complex formation. At higher concentrations of sodium thiosulfate (above 0.2 M) the plot of change of potential of the mercury electrode against the logarithm of the activity of $S_2O_3^{2-}$ becomes nearly a straight line. The experimental points fit on a straight line with an angular coefficient of 0.119. We thus obtain the following value for the number of coordinated groups n:

$$n = \frac{\tan \alpha}{0.0295} = 4.03.$$

Evidently in these conditions a complex anion of the composition $[Hg(S_2O_3)_4]^{6-}$ predominates. The instability constant of this complex may be determined from the equation:

$$\log K = \frac{E_x - E}{0.0295} + 4 \log a_{S_2O_3^{2-}} - \log 236 + \log C_{Hg^{2+}} \gamma_0 - \log C_{Hg^{2+}} \gamma_c \tag{1}$$

where

E_x is the potential of the mercury electrode in the solution of complex salt measured against the saturated calomel electrode;

E is the potential in the absence of sodium thiosulfate at the same initial concentration of Hg^{2+} (in $2 \cdot 10^{-3}$ M solution, E = 0.4759 V);

$a_{S_2O_3^{2-}}$ — is the activity of the thiosulfate ion;

$C_{Hg^{2+}}$ is the initial concentration of divalent mercury ions;

$\gamma_0 \gamma_c$ are the activity coefficients of the simple and complex ions;

Since the activity coefficients of both the simple mercury ions and the complex mercury thiosulfate ions are unknown, calculation was performed by a simplified approximate equation in which we neglected the difference in the activity coefficients of the simple and complex ions.

In the calculations the equilibrium constant of the reaction $Hg^{2+} + Hg \rightleftharpoons Hg_2^{2+}$ was assumed to be 235 [9]

Values of the instability constants calculated from the above-mentioned equations are set forth in Table 3.

For determination of the consecutive instability constants and of the conditions of formation of

the coordinatively unsaturated complexes we made use of Yatsimirsky's method [8].

The equilibrium activities of SO^{2-} were first calculated, applying the concept of the mean coordination number N introduced by Leden [10]. The approximate value of N was found from the graph obtained by plotting the potential of the mercury electrode (E_{Hg}) against the logarithm of the total activity of $S_2O_3^{2-}$ ($\log a_{total}$). In a certain narrow range of concentrations of $S_2O_3^{2-}$ it is possible to distinguish the rectilinear portions. The angular coefficient of these straight lengths must be.

$$\frac{dE}{d\log a_{total}} = \frac{N \cdot 0.0295\, a_{total}}{a_{total} - NC_{Hg^{2+}}}. \qquad (2)$$

We found the following values of the tangents of the angles of slope of three straight lines: 0.120, 0.127, 0.109. From equation (2) N was calculated for each concentration of $S_2O_3^{2-}$ and then, from the N values, the equilibrium activities of $S_2O_3^{2-}$ were determined.

A graph was then plotted from the above data (Figs. 1 and 2) from which, by Yatsimirsky's method, the consecutive instability constants of the thiosulfate complexes of mercury were determined.

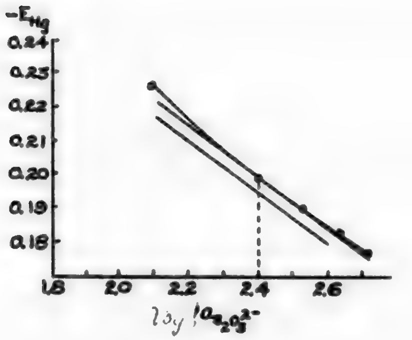

Fig. 1. Dependence of electrode potential on the logarithm of the activity of the complex-forming salt.
(Angular coefficient of tangent = 0.074).

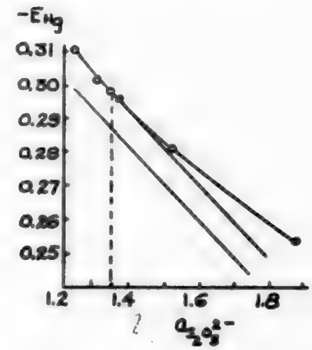

Fig. 2. Dependence of electrode potential on the logarithm of the activity of the complex-forming salt.
(Angular coefficient of tangent = 0.103).

The curve of Fig. 1 covers the region of sodium thiosulfate activities between $1.9 \cdot 10^{-3}$ and $1.6 \cdot 10^{-2}$ molar. The point of its contact with the straight line whose tangent of angle of slope is equal to 0.074 ($2.5 \cdot 0.0295$) corresponds to a $S_2O_3^{2-}$ activity of $4 \cdot 10^{-3}$ mole. This value is equal to the consecutive instability constant of $K_{3,2}$.

Fig. 2 was plotted from data obtained with higher activities of $S_2O_3^{2-}$ (from $1.3 \cdot 10^{-2}$ to $6.8 \cdot 10^{-2}$). In this case the tangent has an angular coefficient of 0.103 ($3.5 \cdot 0.0295$). The point of contact corresponds to a logarithm of the activity of $Na_2S_2O_3$ equal to -1.324. Hence the consecutive instability constant $K_{4,3} = 4.5 \cdot 10^{-2}$. We can now calculate the total instability constants of thiosulfate complexes of mercury:

$$K_3 = \frac{K_4}{K_{4,3}} = 5.5 \cdot 10^{-28},$$

$$K_2 = \frac{K_3}{K_{3,2}} = 1.37 \cdot 10^{-30}.$$

It is not difficult to determine the region of thiosulfate ion concentrations most favorable for existence of each complex. Evidently the complex ion $[Hg(S_2O_3)_2]^{2-}$ preponderates in a solution whose thiosulfate ion concentrations do not exceed $4 \cdot 10^{-3}$ g-ions/l. In the region of sodium thiosulfate concentrations between $4 \cdot 10^{-3}$ and $4.8 \cdot 10^{-2}$ g-ions/l; the dominating complex group is $[Hg(S_2O_3)_3]^{4-}$. At higher sodium

thiosulfate concentrations, a large proportion of the mercury ions are in the form of the complex $[Hg(S_2O_3)_4]^{6-}$.

TABLE 3

Activity of $Na_2S_2O_3$	$E_x - E$	K
$1.06 \cdot 10^{-1}$	-0.8093	$2.46 \cdot 10^{-34}$
$1.24 \cdot 10^{-1}$	-0.8179	$2.50 \cdot 10^{-34}$
$1.71 \cdot 10^{-1}$	-0.8336	$2.46 \cdot 10^{-34}$

TABLE 4

Complex ion	Instability constant
$[Hg(S_2O_3)_4]^{6-}$	$2.5 \cdot 10^{-34}$
$[HgI_4]^{2-}$	$5.2 \cdot 10^{-31}$
$[Hg(CNS)_4]^{2-}$	$1 \cdot 10^{-22}$
$[HgBr_4]^{2-}$	$2.3 \cdot 10^{-22}$
$[HgCl_4]^{2-}$	$1.2 \cdot 10^{-15}$

We were unable to detect the existence of a complex of mercury with one thiosulfate residue. When mercuric oxide or iodide reacts with thiosulfate ions, disappearance of turbidity is observed only when the sodium thiosulfate is added in quantity corresponding to the formation of $[Hg(S_2O_3)_2]^{2-}$ ions. This is also consistent with the data of potentiometric titration [3].

Formation of thiosulfate complexes is characteristic only of ions of divalent mercury. Ions of monovalent mercury do not form a complex with thiosulfate ions either in acid or in alkaline solutions.

Thiosulfate complexes of divalent mercury are stable toward caustic alkalies in solutions. The potential of the mercury electrode remains constant in the pH range of 7.9 to 10.3.

The complex is also stable in acidic solutions. Mercurous sulfate is, however, precipitated on direct interaction of mercury ions with thiosulfate ions in an acid medium. If, however, sodium thiosulfate is added to the mercuric oxide in equivalent amount, then subsequent addition of acid does not lead to breakdown of the complex.

A comparison of the stability of thiosulfate complexes of mercury with the stability of complex thiosulfates of cadmium, zinc and lead show that ions of divalent mercury form the more stable complexes with thiosulfate ions. A comparison of the stability of these complexes with the stability of other known complexes of mercury shows that the thiosulfate residue takes the first place in tendency to complex formation in a series of addends:

$$S_2O_3^{2-} - I^- - CNS^- - Br^- - Cl^-.$$

In Table 4 are set forth the values of the instability constants of some complexes of mercury.

A similar order of arrangement of addends is characteristic of the complexes also formed by other central ions [11, 12].

SUMMARY

1. A potentiometric investigation of thiosulfate complexes of mercury was undertaken.

2. It was shown that in aqueous solutions, ions of divalent mercury form complexes with different numbers of coordinative groups with the thiosulfate ion: $[Hg(S_2O_3)_2]^{2-}$, $[Hg(S_2O_3)_3]^{4-}$ and $[Hg(S_2O_3)_4]^{6-}$.

3. The instability constants of the complexes were calculated.

$$K_2 = 1.37 \cdot 10^{-30},\ K_3 = 5.5 \cdot 10^{-33},\ K_4 = 2.48 \cdot 10^{-34}.$$

4. Thiosulfate complexes of mercury are distinguished by high stability both in comparison with known thiosulfate complexes of other metals and in comparison with known complexes of mercury with other addends.

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DOUBLE DECOMPOSITION IN THE RECIPROCAL SYSTEM OF THE SULFATES AND MOLYBDATES OF SODIUM AND SILVER IN MELTS

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In this paper are presented the results of an investigation by the visual-polythermal method of the surface of crystallization of the ternary reciprocal system Na, Ag || SO_4, MoO_4, which belongs to a series of systems under investigation by one of the authors [1,2,3] involving sulfates and molybdates (tungstates) of alkali metals and metals giving ions with an 18 (Ag) or 18 + 2 (Tl, Pb) electron shell.

EXPERIMENTAL

The procedure has been described before [1,2]. The Na_2SO_4 and Na_2MoO_4 used were chemically pure grades with melting points of 884° and 688°, respectively; the Ag_2SO_4 was prepared by precipitation from $AgNO_3$ solution with sulfuric acid [4], and had m.p. 658°; the Ag_2MoO_4 was prepared by fusing $AgNO_3$ with MoO_3 in the stoichiometric ratio[5] and had m.p. 554°.

All percentages given in the paper are molar.

Binary Systems

The system silver sulfate – sodium sulfate has been studied by Nacken [6]; we made a fresh study of it. It forms continuous solid solutions (Fig. 1). We also repeated the examination of the system sodium molybdate – sodium sulfate, previously studied by Becke [6]. The system is characterized by the presence of a continuous series of solid solutions with a minimum at 673° and 25% Na_2SO_4 (Fig. 1). The system silver molybdate – silver sulfate (Table 1, Fig. 1) is here investigated for the first time. It was found to have a eutectic at 497° and 33% Ag_2SO_4. The system silver molybdate – sodium molybdate (Table 1, Fig. 1) is likewise here investigated for the first time. It is characterized by the presence of a continuous series of solid solutions with a minimum at 546° and 21% Na_2MoO_4.

Diagonal Sections

The silver molybdate – sodium sulfate section (Table 1, Fig. 1) has the form of a simple binary system with a eutectic at 547° and 5.5% Na_2SO_4. The character of the fusibility diagram indicates that this section is a stable diagonal section of the reciprocal system. The silver sulfate – sodium molybdate section (Table 1, Fig. 1) also consists of two crystallization branches and resembles the usual binary systems, but here the intersection of these branches is not eutectic in character, and the crystallization branch starting from Ag_2SO_4 first drops slightly, and then rises steeply to form a ridge of the stable solid solutions (Na, Ag)SO_4. Consequently, the section is not stable, since it intersects the field of the product of decomposition – sodium sulfate – with which silver sulfate forms a continuous series of solid solutions.

Internal Cuts

For clarification of the character of the interaction within the reciprocal system, the distributions of the lines of common crystallization and of the projection of the fields of crystallization of 15 internal cuts were studied in several directions. The fusion data for the cuts are set forth in Table 2 (Figs. 2 and 3). The fusibilities of the side lines, diagonal sections and a fairly large number of internal cuts permitted sufficiently accurate delineation of the surface of crystallization of the system (Fig. 4). The isotherms through 25° are plotted for a more informative representation of the surface of crystallization on the orthogonal projection (Fig. 4).

From Fig. 4 we see that the system studied belongs to the irreversible-reciprocal type [9] with a stable diagonal section of $Ag_2MoO_4 - Na_2SO_4$, although the deviation of the ridge from the stable diagonal and the course of the isotherms in the (Na, Ag)SO_4 field point to a certain reversibility of the reaction

$$Ag_2SO_4 + Na_2MoO_4 \rightleftharpoons Ag_2MoO_4 + Na_2SO_4.$$

The largest field of crystallization in the system belongs to the most stable solid solutions of (Na, Ag)SO_4, while the smallest field of crystallization belongs to the less stable solid solutions of (Na,Ag)MoO_4

TABLE 1

Lateral and Diagonal Sections

1st column—added component; 2nd column % of added component 3rd column—temp. of appearance of first crystals

1	2	3
$Ag_2MoO_4-Ag_2SO_4$		
Ag_2SO_4	0	554
	5	550
	10	541
	15	534
	20	524
	25	514
	30	505
	32.5	498
	35	500
	37.5	505
	40	509
	45	519
	50	526
	55	535
	60	544
	65	555
	70	564
	75	576
	80	590
	85	603
	90	620
	95	637
	100	658
$Ag_2MoO_4-Na_2MoO_4$		
Na_2MoO_4	0	554
	5	553
	10	550
	15	548
	17.5	547
	20	546
	22.5	546
	25	548
	27.5	550
Na_2MoO_4	30	553
	32.5	560
	35	566
	40	580
	45	597
	50	611
	55	622
	60	632
	65	640
	70	648
	75	656
	80	662
	85	668
	90	674
	95	681
	100	688
$Ag_2MoO_4-Na_2SO_4$		
Na_2SO_4	0	554
	2.5	550
	5	548
	7.5	587
	10	638
	15	692
	20	728
	25	753
	30	770
	35	779
	40	784
	45	787
	50	791
	55	794
	60	797
	65	801
Na_2SO_4	70	807
	75	815
	80	826
	85	839
	90	853
	95	869
	100	884
$Ag_2SO_4-Na_2MoO_4$		
Na_2MoO_4	0	658
	5	657
	10	659
	15	665
	20	674
	25	694
	30	720
	35	746
	40	769
	45	782
	50	791
	52.5	790
	55	786
	60	770
	65	740
	70	699
	72.5	676
	75	657
	77.5	647
	80	649
	82.5	652
	85	658
	90	668
	95	677
	100	688

The line of common crystallization, dividing the system into two parts, extends from the eutectic on the side line of $Ag_2SO_4-Ag_2MoO_4$ nearly to the side of $Na_2SO_4-Na_2MoO_4$. The close approach of the line of common crystallization to the $Na_2SO_4-Na_2MoO_4$ side points to the instability of solid solutions of $Na_2(MoO_4, SO_4)$ inside the reciprocal system and to their breakdown under the influence of the silver ion to form the more stable solid solutions of $(Ag, Na)SO_4$ and $(Na, Ag)MoO_4$.

Attention should be directed to the fact that in the binary systems $Na_2SO_4-Na_2MoO_4$ and $K_2SO_4-K_2MoO_4$ continuous series of solid solutions are formed, whereas in the systems $Ag_2SO_4-Ag_2MoO_4$ (studied by us) and $PbSO_4-PbMoO_4$ [6] a continuous series of solid solutions is not formed, just as chromates and molybdates of sodium and chromates and molybdates of potassium [6] form continuous series of solid solutions

while in the system of lead chromate and molybdate there is limited solubility in the solid state with a eutectic.

It is interesting to compare the system Ag, Na ‖ SO_4, MoO_4 with the previously studied systems

TABLE 1

Summarized Data for the Internal Cuts: A) Na_2MoO_4, B) Ag_2MoO_4, C) Na_2SO_4, D) Ag_2SO_4, E) (Na, Ag)MoO_4, F) $Na_2(MoO_4, SO_4)$, G) (Na, Ag)SO_4.

No. of cut	Initial mixture in %	M.p. of starting mixture	Component added	Branches of crystallization curves: Branch 1	Intersection of branches 1 and 2: %	Intersection of branches 1 and 2: Temp.	Branch 2
I	87.5 A 12.5 B	670°	C	F	–	–	–
II	57.5 A 42.5 B	626	C	E	14	625°	G
III	42.5 A 57.5 B	589	C	E	3.5	587	G
IV	25 A 75 B	548	C	E	1.5	546	G
V	12.5 A 87.5 B	549	C	E	1.0	547	G
VI	87.5 B 12.5 D	538	C	E	3.5	531	G
VII	70 B 30 D	505	C	E	1.0	504	G
VIII	62.5 B 37.5 D	505	A	G	63.0	624	E
IX	55 B 45 D	519	C	G	–	–	–
X	47.5 B 52.5 D	529	A	G	68.0	633	E
XI	35 B 65 D	555	A	G	71.0	637	E
XII	15 B 85 D	603	A	G	74.0	643	E
XIII	75 D 25 C	733	A	G	73.5	652	E
XIV	50 D 50 C	791	A	G	70.5	658	E
XV	25 D 75 C	832	A	G	66.5	665	E

of Na, Pb ‖ SO_4, MoO_4 [1] and Na, Pb ‖ SO_4, WO_4 [2], in which the solid solutions of $Na_2(SO_4, MoO_4)$ and $Na_2(WO_4, SO_4)$ do not break down even inside the reciprocal systems. The very low stability of solid solution of $Na_2(MoO_4, SO_4)$ in the system Ag, Na ‖ SO_4, MoO_4 indicates a differing influence of the Ag and Pb ions upon the stability of the solid solutions. It is possible that this is associated with the presence in the system Na, Ag ‖ SO_4, MoO_4, of the more stable solid solutions of (Na, Ag)MoO_4, (Na, Ag)SO_4, in which the difference in the dimensions of the Na and Ag ions is considerably less than the difference between the SO_4'', MoO_4'' ions in

systems [1,2], on the $Na_2SO_4-PbSO_4$ and $Na_2MoO_4-PbMoO_4$ sides of which there are no continuous series of solid solutions.

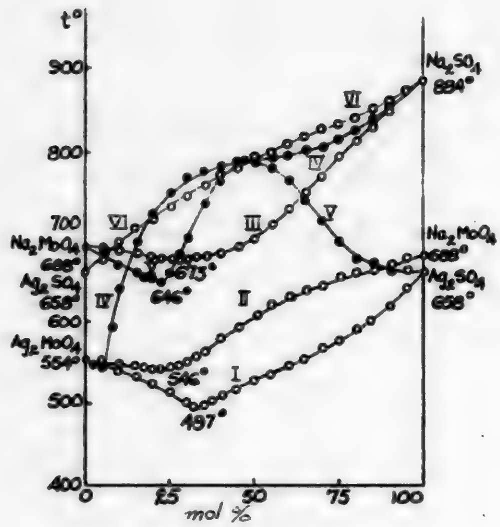

Fig. 1. Fusibility diagram.
I) B – G, II) B – A, III) A – C, IV) B – C, V) A – D, VI) D – C.
Explanation in text and Table 2.

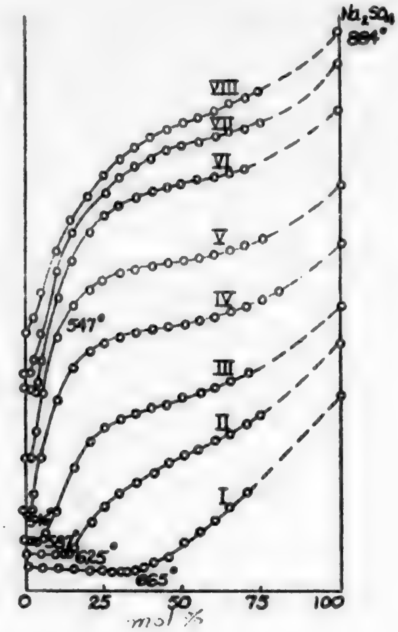

Fig. 2. Fusibility of sections through the reciprocal system.
Explanation in text and Table 2.

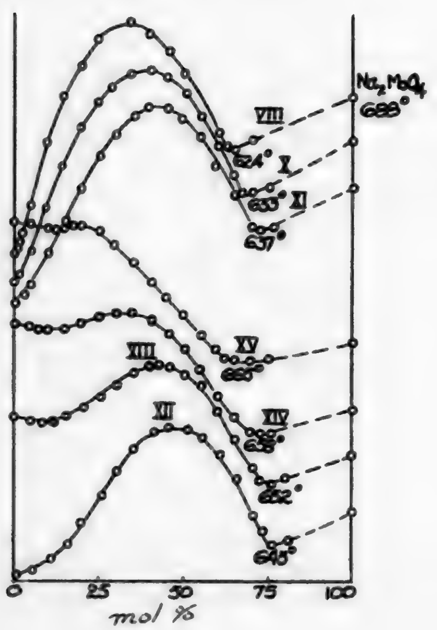

Fig. 3. Fusibility of sections through the reciprocal system
Explanation in text and Table 2.

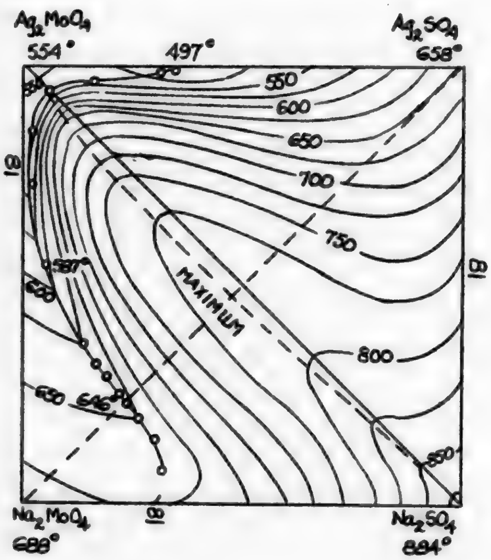

Fig. 4. Orthogonal projection on to the square of compositions of the system Na, Ag || SO_4, MoO_4

In the systems Na, Pb || SO_4, MoO_4 and Na, Pb || SO_4, WO_4 the equilibrium is shifted to the side of the pair of salts, one of which contains a cation with an 18 + 2 electron shell and an anion containing an element with an incomplete d-electron shell (W, Mo)—(Na_2SO_4—$PbWO_4$ and Na_2SO_4—$PbMoO_4$); in the system Ag, Na || MoO_4, SO_4 the equilibrium is displaced to the side of the pair of salts, one of which contains a cation with an 18-electron shell (Ag) and an anion containing an element with an incomplete d-electron shell (Mo). This enables us to state that, in general, in ternary reciprocal systems in which there is one cation with an 18 + 2 (Tl, Pb) or 18 (Ag) external electron shell, and in which one anion contains an element with an incomplete d-electron shell (Mo, W), the equilibrium is shifted in the direction of the pair of salts, one of which contains a cation with an 18- or 18 + 2-external electron shell and an anion with an incomplete d-shell ($PbMoO_4$, Pb WO_4, Ag_2MoO_4).

In the second of the two systems compared, the largest crystallization surface is possessed by $PbMoO_4$, $PbWO_4$; in the first, on the contrary, the largest surface belongs to Na_2SO_4; this inversion is in close harmony with the rules given in the literature [7, 8]. In arrangement and character of the fields of crystallization, the system here studied is similar to the system Na, Ag || Br, I [8].

SUMMARY

1. Using the visual-polythermal method, a study has been made for the first time of the binary systems Na_2MoO_4—Ag_2MoO_4 and Ag_2SO_4—Ag_2MoO_4. In the first are formed continuous solid solutions of (Na, Ag)MoO_4 with a minimum at 546° and 21% Na_2MoO_4, while the second gives a eutectic at 497° and 33% Ag_2SO_4.

2. The surface of crystallization of the ternary reciprocal system Na, Ag SO_4, MoO_4 was studied. It was shown that the system belongs to the irreversible-reciprocal type with the stable diagonal section of Na_2SO_4—Ag_2MoO_4.

3. It was established that inside the reciprocal systems the silver ion has a considerably greater influence on the stability of solid solutions of $Na_2(MoO_4, SO_4)$, than the lead ion.

4. The hypothesis is advanced that in ternary reciprocal systems with participation of one cation with an 18- or 18 + 2- external electron shell and one anion containing an element with an incomplete d-electron shell, the equilibrium is shifted in the direction of the pair of salts, one of which also contains a cation with an 18- or 18 + 2- electron shell and an anion containing an element with an incomplete d-electron shell.

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*** See Consultants Bureau Translation, page 451.

PREPARATION OF PURE VANADYL CHLORIDE SOLUTION

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A method is described in the literature [1] for the preparation of solutions of vanadyl sulfate and vanadyl chloride by the action of metallic mercury on an acidified solution of ammonium vanadate. Removal from the solution of ions of the resultant univalent mercury is effected by adding – in the case of sulfate solutions – potassium chloride or sodium chloride in quantity slightly in excess of the calculated quantity. These processes may be expressed by the following equations:

$$2HVO_3 + 2Hg + 3H_2SO_4 = 2VOSO_4 + Hg_2SO_4 + 4H_2O;$$

$$2HVO_3 + 2Hg + 6HCl = 2VOCl_2 + Hg_2Cl_2 + 4H_2O.$$

Actually, from a comparison of the normal oxidation-reduction potentials of the two systems:

$$E_{0\,VO^{2+} + 3H_2O | V(OH)_4^+ + 2H^+} = 1V \text{ and } E_{0\,2Hg + 2Cl^- | Hg_2Cl_2} = 0.2627 \text{ V},$$

we see clearly that the reduction of vanadium from the quinquevalent to the quadrivalent state proceeds almost completely under the action of metallic mercury in presence of chlorine ions.

The method proposed by the authors cited, however, is not free from defects: use of ammonium vanadate as starting material is bound to lead to the introduction of ammonium ions into the solution of vanadium salt. Moreover, when preparing a solution of vanadyl sulfate, the presence of potassium or sodium ions is inevitable, as is also a small quantity of chlorine ions.

We used* freshly precipitated vanadium pentoxide as starting material with the objective of eliminating these defects and obtaining a pure solution of vanadyl chloride. To a hot, nearly saturated ammonium vanadate solution containing about 50 g salt in 900 ml water was added 100 ml dilute hydrochloric acid (1:3). The precipitated V_2O_5 was filtered off and washed with hot water acidified with hydrochloric acid.

A pure vanadyl chloride solution was prepared by adding to a beaker, containing hydrochloric acid solution of a definite concentration, vanadium pentoxide in quantity determined from the required content of vanadyl ion in the solution; metallic mercury was added in excess and the mixture was agitated for 5-10 minutes. After filtering off the precipitate of residual mercury and of the calomel formed, a pure solution of vanadyl chloride was obtained.

Complete reduction of the vanadium to the quadrivalent form was effected by the following procedure: 25 ml of the obtained solution was pipeted off and 10 ml H_2SO_4 and 10 ml Reinhardt mixture were added to it; the mixture was heated to 60° and titrated with potassium permanganate to a pink color which persisted for 1 minute.

To another equal portion of the solution was added 10 ml H_2SO_4 and a stream of sulfur dioxide was passed through while heating on a water bath; the excess of sulfur dioxide was eliminated by passing carbon dioxide (test by cessation of decolorization of acidified permanganate solution with the evolved gas). After 10 ml Reinhardt mixture had been added, titration was performed with permanganate. The good reproducibility of the results showed that the metallic mercury had substantially reduced VO_3^- to VO^{2+}.

Expt. No.	Amount of V_2O_5 suspension (in ml)	Normality of HCl	$KMnO_4$ consumed in titration (in ml): after reduction of Hg	after supplementary reduction with SO_2
1	2	0.5	2.20	2.30
2	2	0.1	2.40	2.46
3	5	0.1	6.15	6.10
4	5	0.1	6.95	6.95
5	10	0.05	4.80	4.85
6	10	0.05	4.60	4.66

Note: The difference between experiments 1-2, 3-4 and 5-6 is accounted for by the difference in V_2O_5 content of the suspension.

* A. A. Ryzh participated in the experimental work.

All these experiments were carried out with 1 N hydrochloric acid. Desiring to obtain vanadyl chloride solutions of lower acidity, we prepared a suspension of vanadium pentoxide in solutions of hydrochloric acid of the following concentrations: 0.5, 0.1, 0.05 and 0.01 N. Experimental results are set forth in the table.

The data show that substantially complete reduction of vanadium by mercury is effected even in 0.05 N HCl. When using 0.01 N solution, however, the absence of complete reduction was evident from the color of the solution. This is undoubtedly a defect of the method.

SUMMARY

1. An improved method is proposed for the preparation of pure solutions of vanadyl chloride by reduction of freshly precipitated vanadium pentoxide with metallic mercury.

2. It was established that the lowest acidity that can be attained is 0.05 N.

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CRACKING OF NORMAL PARAFFINIC HYDROCARBONS IN PRESENCE OF ALUMINUM CHLORIDE

II. CRACKING OF n-HEXADECANE

L. A. Potolovsky and G. S. Spektor

The cracking of low-molecular normal paraffinic hydrocarbons (from C_5 to C_8) in presence of aluminum chloride has been extensively studied in numerous investigations. The cracking of normal paraffinic hydrocarbons of higher molecular weights has hardly been studied. Only some isolated papers have been published and we have previously drawn attention to them [1]. Gault and Sigwalt [2] have described the cracking of n-hexadiene in presence of $AlCl_3$. They obtained propane, butane and higher boiling hydrocarbons which were not investigated in detail. Bauer and Toma [3] cracked octadecane and hexatriacontane in presence of 25% $AlCl_3$ and obtained low-molecular paraffinic hydrocarbons about whose structure no information was given.

In the present investigation, n-hexadecane* was cracked in the apparatus which we previously described at atmospheric pressure in presence of HCl in the temperature range of 150-250°, using 5 to 15% $AlCl_3$. The temperature in the glass-packed column was maintained at 110-120°.

The composition and yield of gaseous products of cracking of n-hexadecane are set forth in Table 1.

TABLE 1

Composition and Yield of Gaseous Products of Cracking of n-Hexadecane in Presence of $AlCl_3$ (in weight %)

Conditions	Number of experiment				
	1	2	3	4	5
Temperature	100	150	200	200	250
Weight percentage of $AlCl_3$	15	15	15	7.5	5
Duration in hours	8	8	4	6	9
Extent of conversion	53.8	58.5	100	73.5	73.9
Composition of gas:					
H_2	Traces	Traces	Traces	Traces	Traces
CH_4	1.2	0.7	0.7	1.5	Traces
C_2H_6	0.4	0.0	0.1	0.8	0.0
C_3H_8	0.5	2.5	6.0	2.2	9.1
iso-C_4H_{10}	96.0	96.8	93.2	95.5	88.6
n-C_4H_{10}	1.9	0.0	0.0	0.0	2.3
Yield of gas:					
on the original n-hexadecane	15.0	19.4	33.4	25.0	24.2
on the reacted n-hexadecane	27.9	33.1	33.4	34.0	32.8

The main component of the gas, as in the case of cracking of n-heptane and n-nonane, is isobutane. The gases resulting from the cracking of hexadecane contain, however, a larger amount of propane (up to 9 wt.-% of the gas). The yield of propane, as in the case of cracking of n-heptane and n-nonane, increases with the cracking temperature (Experiments 1, 2, 3, 5). An increase in the quantity of $AlCl_3$ introduced into the reaction also increases the yield of propane (Expts. 3 and 4).

The material balance of the products of cracking of n-hexadecane is given in Table 2, which indicates that the main bulk of the liquid products of cracking boils up to 100°. Hydrocarbons boiling at higher temperatures are obtained in low yields (1.3-3.8% reckoned on the original hydrocarbon).

* n-Hexadecane was obtained by recrystallization of standard cetane [4]. The initial temperature of crystallization was 17.85°; b.p. 286°; d_4^{20} 0.7735; n_D^{20} 1.4350.

TABLE 2

Yield of Products of Cracking of n-Hexadecane in Presence of $AlCl_3$ (in percentages by weight)

Conditions	Number of experiment				
	1	2	3*	4	5
Temperature	150°	200°	200°	200°	250°
Weight-% $AlCl_3$	15	15	10	7.5	5
Duration (in hours)	8	4	16	6	9
Gas	19.4	33.4	14.9	25.0	24.2
Including:					
iso-C_4H_{10}	18.8	31.2	–	23.9	21.4
Fractions:					
27-29°	10.5	19.1	10.3	14.6	14.6
29-38°	1.1	0.5	0.3	0.2	0.4
38-64°	6.9	12.8	7.9	10.2	10.5
64-77°	0.8	1.2	0.9	1.1	0.8
77-94°	0.7	6.9	4.6	5.2	4.5
94-100°	0.5	1.0	3.8***	0.3	–
100-120°	–	2.7	–	0.6**	1.3
120-284°	1.5	–	–	2.4	0.5
284-286°	41.4	–	46.6	26.5	26.1
Hydrocarbons combined with $AlCl_3$ in residue after cracking	17.2	22.4	10.7	13.9	17.1
Total percentage decomposition of original hydrocarbon	58.6	100.0	53.4	73.5	73.9

After 8 hours at 150°, n-hexadecane is only converted to the extent of 58.6%. When the temperature is raised to 200° (Expt. 2) it is completely cracked in 4 hours. Reduction of the quantity of $AlCl_3$ from 15 to 7.5% (Expt. 4) lowers the conversion after 6 hours to 73.5%. Attainment of the same percentage decomposition as in Expt. 4 when using 5% $AlCl_3$ (Expt. 5) requires a rise of temperature to 250° and a reaction duration of 9 hours.

TABLE 3

Hydrocarbon Composition of Fractions Obtained by Cracking of n-Hexadecane, determined by the Raman method****

Hydrocarbon composition (in percentages by wt.)	Number of experiment					
	2		4		1, 2, 3, 4, 5	
	Boiling limits of fractions (in °)					
	38-64	77-94	27-38	38-64	77-94	64-77*****
Isopentane	–	–	100	–	–	–
n-Pentane	–	–	–	–	–	–
2-Methylpentane	60	–	–	70	–	–
3-Methylpentane	12	–	–	20	–	30
2,2-Dimethylbutane	3	–	–	–	–	–
2,3-Dimethylbutane	15	–	–	–	–	–
n-Hexane	10	–	–	10	–	13
2-Methylhexane	–	50	–	–	35	–
3-Methylhexane	–	22	–	–	20	–
2,4-Dimethylpentane	–	20	–	–	13	50
2,3-Dimethylpentane	–	–	–	–	27	–
2,2,3-Trimethylbutane	–	8	–	–	5	7

* Experiment in absence of HCl

** Fraction 100-107°.

*** Fraction 94-284°.

**** The analysis was carried out in the laboratory of molecular spectroscopy of Moscow State University under the direction of V. M. Tatevsky.

***** The 64-77° fractions from these experiments were combined.

Introduction of hydrogen chloride into the reaction zone considerably speeds up the cracking reaction in presence of $AlCl_3$; thus, in presence of HCl (1-1.1%) and 7.5% $AlCl_3$ with a duration of experiment of 6 hours, the percentage conversion is 73.5; in the absence of HCl and using 10% $AlCl_3$, the n-hexadecane is only 53.4% converted after 16 hours.

The chemical composition of the liquid products of cracking of n-hexadecane, boiling up to 100°, is determined on the basis of data for fine rectification, for the physical constants of the fractions* and for the Raman spectra (Table 3). Their main components are isopentane, isohexanes and isoheptanes, i.e., the same products as in the case of cracking of n-heptane and n-nonane [1].

The pentane fraction is pure isopentane; n-pentane was found in traces. The main component of the isohexane fraction is 2-methylpentane, that of the isoheptane fraction is 2-methylhexane. Very much smaller amounts of isomers with the methyl group in the 3-position are formed (up to 20% of the fraction); the same is true of isomers with 2-methyl groups in the 2,3- and 2,4-positions (up to 15%). Hydrocarbons containing a quaternary carbon atom are formed in still smaller quantity (from 3% to 8% on the fraction).

Independently of the experimental conditions, the yield of the main components of the products of cracking of n-hexadecane are in decreasing order from isobutane to isopentane (Table 4).

TABLE 4

Yield of Isoparaffinic Hydrocarbons in Cracking of n-Hexadecane (in percentages by weight of the reacted hydrocarbon)

Expt. No.	Conditions of experiment: Temp.	$AlCl_3$ (in wt.-%)	duration (in hrs.)	Degree of conversion	Isobutane	Isopentane	Isohexanes	Isoheptanes
1	150°	15	8	58.6	32.2	19.7	11.1	2.1
2	200	15	4	100	31.2	19.6	11.9	7.6
3**	200	10	16	53.4	—	19.8	13.8	9.5
4	200	7.5	6	73.5	32.4	20.2	12.8	7.8
5	250	5	9	73.9	29.0	20.3	13.1	6.7

TABLE 5

Characterization of Products of Cracking of n-Hexadecane Boiling above 100°

Expt. No.	Expt. conditions: temperature	$AlCl_3$ (in wt.-%)	duration (hrs.)	Boiling range of fractions	d_4^{20} before sulfonation	d_4^{20} after sulfonation	n_D^{20} before sulfonation	n_D^{20} after sulfonation	Critical temp. of solution in aniline after sulfonation *****	Hydrocarbons sulfonated (in wt.-%)	Specific dispersion
6	200°	15	4	100-120°****	0.7072	0.7066	1.3989	1.3990	71.7°	0.5	—
3***	200	10	16	207-284	0.7942	0.7935	1.4418	1.4400	89.2	2.0	100.5
4	200	7.5	6	100-107	0.7000	—	1.3960	—	—	—	—
4	200	7.5	6	107-246	0.7957	0.7930	1.4400	—	71.7	7.0	—
4	200	7.5	6	246-284	0.7848	0.7840	1.4371	1.4373	91.6	5.0	—
7	100	15	8	129-284	0.7872	—	1.4400	—	—	—	100.4
1	150	15	8	100-284	0.8542	—	1.4638	—	—	—	100.8
2	200	15	4	100-125	0.7208	—	1.4065	—	—	—	—

* Fractions: 1) 27-38°: d_4^{20} 0.6190-0.6195, n_D^{20} 1.3537-1.3539;
2) 38-64°: d_4^{20} 0.6551-0.6557, n_D^{20} 1.3727-1.3734;
3) 64-77°: d_4^{20} 0.6697-0.6707, n_D^{20} 1.3805-1.3810;
4) 77-94°: d_4^{20} 0.6831-0.6842, n_D^{20} 1.3872-1.3880.

** Experiment in absence of HCl.

*** Experiment in absence of HCl.

**** Residue after rectification (boiling range determined by distillation of residue from a Würtz flask of 5 ml capacity).

***** Sulfonation carried out with three volumes of 98% H_2SO_4.

The data of Table 4 show that in the temperature range 200-250° the yields of the main components of the products of cracking remain nearly constant when calculated on the reacted hydrocarbon. It would, therefore, appear that in this temperature range, the quantity of $AlCl_3$ and the presence of HCl are factors that only govern the velocity of the cracking reaction, but not the composition of final products.

Investigation of the products boiling above 100°, formed by cracking of n-hexadecane, showed that they are paraffinic hydrocarbons (Table 5) and similar in chemical composition to the high-boiling products of cracking of n-heptane and n-nonane [1].

An examination was also made of the hydrocarbons isolated from the residues obtained in the cracking of n-heptane, n-nonane and n-hexadecane in presence of $AlCl_3$. The isolation of these hydrocarbons, chemically combined with the $AlCl_3$ in the process of cracking, was effected by decomposing the residues with water in an atmosphere of carbon dioxide while cooling with ice.

The hydrocarbons separated in this manner from residues formed at experimental temperatures of 50 to 150° were dark oils, while the product formed at 200-250° (in the case of n-hexadecane) was a hard, powdery substance.

The isolated liquid hydrocarbons were dissolved in benzene and the solvent was distilled off at reduced pressure (residual pressure 30-35mm). The solid hydrocarbons (the pulverulent material) were transferred to a filter, washed with water until neutral and dried in a current of carbon dioxide. Results are set forth in Table 6. The remarkably high iodine numbers (222-306) and empirical formulas, calculated on the basis of the elementary composition and molecular weight), show that the bottom layer of cracked products contains highly unsaturated and polycyclic hydrocarbons.

TABLE 6

Characterization of Hydrocarbon Portion of Residues after Cracking of n-Paraffinic Hydrocarbons in Presence of $AlCl_3$ for 8 hours

Starting hydrocarbon	Experimental conditions		Molecular weight *	Iodine number **	Elementary composition (%)		Empirical formula
	temp.	$AlCl_3$ (wt.-%)			H	C	
n-Heptane	100°	20	305	302	11.23	88.54	$C_{22}H_{34}(C_nH_{2n-10})$
	50	10	287	302	12.00	87.25	$C_{21}H_{34}(C_nH_{2n-8})$
	100	10	298	292	11.63	88.23	$C_{22}H_{35}(C_nH_{2n-9})$
n-Nonane	150	10	308	306	10.47	88.86	$C_{23}H_{32}(C_nH_{2n-14})$
n-Hexa-decane	100	15	301	221	11.55	88.31	$C_{21}H_{33}(C_nH_{2n-9})$
	150	15	347	253	10.0	89.39	$C_{26}H_{34}(C_nH_{2n-18})$

Unsaturated hydrocarbons are not present among the products of cracking of n-paraffinic hydrocarbons found in the upper layer. Formation on the one hand of saturated hydrocarbons and on the other hand of hydrocarbons with an extremely low hydrogen content (in the lower layer) must have involved a process of hydrogen rearrangement in which a portion of the hydrocarbons (low-molecular) becomes saturated with hydrogen at the expense of dehydrogenation of the high-molecular portion. This reaction is characteristic not only of the cracking of n-paraffinic hydrocarbons in presence of HCl but also of the cracking of other classes of hydrocarbons in presence of various catalysts [5, 6, 7]. Rise of cracking temperature and an increased amount of $AlCl_3$ lead to diminution of the hydrogen content of the hydrocarbon residue.

SUMMARY

1. The main products of cracking of n-hexadecane in presence of $AlCl_3$ are isoparaffinic hydrocarbons. Their yields fall off from isobutane to isoheptane regardless of the experimental conditions. Isomers with a methyl group in the 2-position are predominantly formed; those with a methyl group in the 3-position and with two methyl groups are formed in smaller quantities. Isomers with a quaternary carbon atom are also formed in small amount.

Low molecular paraffins of normal structure are formed in insignificant amounts.

* By cryoscopic method.

** By Hübl -Waller method.

2. The gaseous products of cracking consist mainly of isobutane (88-96%); the yield of propane (on the total gas) reaches 9%. The propane yield increases with rising experimental temperature and with increasing amount of $AlCl_3$. Methane and ethane are formed in very minor amounts (0.7-2.3%).

3. Hydrocarbons boiling above 100° are formed in small amounts (up to 4%); they are paraffins.

4. The quantity of $AlCl_3$ and the presence of HCl in the 200-250° temperature range do not affect the composition of the final products of cracking of n-hexadecane, but they govern the reaction velocity.

5. The hydrocarbons isolated from the residues of cracking of n-heptane, n-nonane and n-hexadecane in presence of $AlCl_3$ are highly unsaturated compounds.

6. The similarity in composition of theproducts of cracking of n-heptane, n-nonane and n-hexadecane in presence of $AlCl_3$ testifies to the similarity of the mechanism of decomposition of normal paraffinic hydrocarbons of differing molecular weight in the conditions studied.

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* See Consultants Bureau Translation, page 225.

THE HYDROGEN BOND AND THE PHYSICAL PROPERTIES OF SOME SUBSTITUTED PHENOLS AND ANISOLES

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Formation of a hydrogen bond in a molecule or between molecules leads to a marked change in their properties. Characteristics of these changes for infra-red and Raman spectra [1], for absorption in the ultraviolet and in the visible spectrum [2], and for the dipole moments of molecules [3] have been established. The data for different molecules, however, lead to conflicting conclusions regarding the character of the association of some substituted phenols and anisoles, in particular pyrocatechol, guaiacol and o-anisidine.

Pyrocatechol, for example, unlike other compounds with an intramolecular hydrogen bond, exhibits intense absorption in the region of the first harmonic and fundamental vibration frequencies of the isolated OH group [4] and absorbs in a shorter wave region of the ultraviolet than its para-isomer [5]. Data for the dipole moments [6] and some chemical properties of pyrocatechol [7] point to great stability of its intramolecular hydrogen bond. Similarly in the case of guaiacol the infra-red spectrum exhibits intense absorption in the region of vibration frequencies of the isolated OH group [4, 8]. Results of measurements of the dipole moments [9], however, led to the conclusion that the guaiacol molecule contains an intramolecular bond whose stability is even higher than that of o-hydroxyacetophenone.

Evidently, the data for the various properties of the molecules of the above-mentioned substances do not allow of a definite answer to the question of the character and stability of their association. Since for compounds with inter- and intramolecular hydrogen bonds a series of characteristics of their physical properties have been established (boiling point [10], density, surface tension and viscosity in the liquid state [11]), it is natural to compare the physical properties of dihydroxybenzenes and their ethers with the aim of determining the character and stability of the association in pyrocatechol and guaiacol. In Table 1, are set for the results of measurments of the density, viscosity and surface tension of these compounds in the liquid state at two temperatures (131 and 184°); data are also given for their boiling points.

TABLE 1

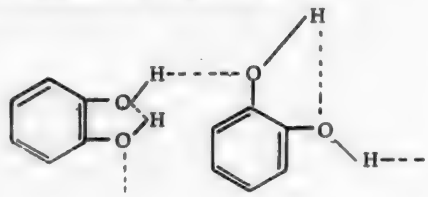
Physical Properties of Dihydroxybenzenes and Their Ethers

Compound		Density at		Surface tension at		Viscosity ($\eta \cdot 10^3$)		B.p. at
		131°	184°	131°	184°	131°	184°	760 mm
Dihydroxybenzene:	o-	1.137	1.071	36.5	32.0	18.09	8.41	245°
	m-	1.165	1.110	45.4	41.6	46.39	15.73	276
	p-	—	—	—	—	—	—	286
Methoxyphenol:	o-	1.022	0.953	28.8	23.8	6.43	3.97	205
	m-	1.052	0.990	33.6	29.3	—	5.36	244
	p-	1.060	0.999	34.2	29.9	13.44	6.88	243
Dimethoxybenzene:	o-	0.981	0.908	26.0	22.6	5.46	3.53	207
	m-	0.965	0.902	25.9	21.9	6.82	4.19	215
	p-	0.972	0.904	26.3	21.7	5.09	3.40	212

It follows from the above data that guaiacol, like all compounds with an intramolecular hydrogen bond, possesses exceptionally low values of all the properties enumerated in comparison with those of the isomers; in the case of the dimethyl ether, the lowering of the constants is much less marked than in the isomers (there is even a rise of boiling points); in contrast to the isomers, guaiacol possesses a lower surface tension and viscosity than the original phenol (at 131°, the surface tension of phenol is 30.0 erg/cm^2, the viscosity is $7.25 \cdot 10^3$ poises); compared with anisole, there is a rise of density almost identical with the increase of molecular weight, whereas in the isomers as in all intermolecularly associated compounds, the rise of density exceeds the increase of molecular weight. Hence, guaiacol both at 131° and 184° behaves like a compound with an intramolecular hydrogen bond. This also follows from the fact that it differs from its isomers in possessing a lower boiling point than its isolog —thioguaiacol; it also has an appreciably lower density and boiling point than its metamer —homopyrocatechol. A portion of the guaiacol

molecules are evidently, nevertheless, intermolecularly associated, for in the series of isoperiodic compounds (compounds differing from one another not only in the number of hydrogen atoms, but also in containing atoms of elements in the same period of the periodic system) guaiacol deviates slightly in b.p. and other properties from the value corresponding to its dipole moment.

Pyrocatechol, likewise, manifests some of the above-mentioned features which are characteristic of compounds with an intramolecular hydrogen bond. Thus, it possesses appreciably lower values of all the above properties in comparison with resorcinol; unlike the latter it differs from phenol in the absence of an increasing density with rising molecular weight. In addition, however, pyrocatechol also manifests qualities characteristic of compounds which are intermolecularly associated through hydrogen bonds. Thus, in comparison with its monomethyl ether it possesses much higher values of all constants than does thiopyrocatechol; unlike guaiacol and the similarly intermolecularly associated cresols and benzyl alcohol, pyrocatechol has an anomalously high boiling point in the series of isoperiodic compounds (Fig. 2). Pyrocatechol must evidently be classed with the compounds which in the liquid state are of the mixed-associated type, i.e., both inter- and intramolecularly associated:



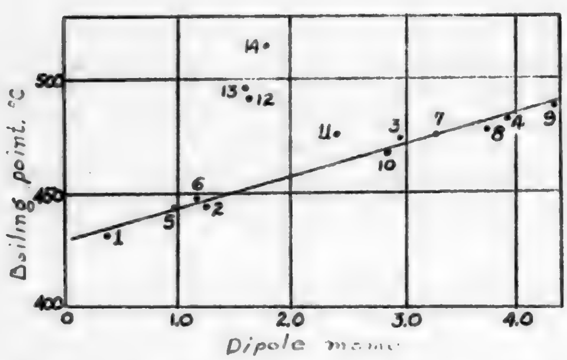


Fig. 1. 1) $C_6H_5C_3H_7$; 2) $C_6H_5OC_2H_5$; 3) $C_6H_5COCH_3$; 4) $C_6H_5NO_2$; 5) $C_6H_4(CH_3)OCH_3$-o; 6) $C_6H_4(CH_3)OCH_3$-p; 7) $C_6H_4(CHO)CH_3$-p; 8) $C_6H_4(CN)CH_3$-o; 9) $C_6H_4(CN)CH_3$-p, 10) $C_6H_4(CHO)OH$-o; 11) $C_6H_4(OCH_3)OH$-o; 12) $C_6H_5CH_2CH_2OH$; 13) $C_6H_4(OCH_3)NH_2$-o; 14) $C_6H_4(OCH_3)NH_2$-p.

TABLE 2

Physical Properties of Anisidines at 131°

Compound	Density d_4^{131}	Surface tension (ergs/cm²)	Viscosity ($\eta \cdot 10^3$)
Anisidine:			
o-	0.996	31.3	7.17
m-	0.997	33.0	–
p-	1.003	33.7	8.42

In Table 2 are set forth the results of measurements of density, viscosity and surface tension at 131° of o-, m- and p-anisidines.

It follows from the data that o-anisidine at 131° differs from pyrocatechol and guaiacol in behaving like a compound which does not possess an intramolecular hydrogen bond. An examination of the literature data for density and viscosity of o- and p-anisidines at 55° [12] and their density at 90° [13], nevertheless, offers evidence that at low temperatures the amino group in o-anisidine forms a hydrogen bond with the neighboring methoxy group. This bond, however, appears to be thermally unstable and is readily broken by heating with consequent appreciable reduction of the difference in the physical constants of the isomers at 131°. At this temperature, o-anisidine resembles its isomers in behaving like an intermolecularly associated compound. This also follows from the extent of depression of the boiling point of o-anisidine, as well as of its isomers, on conversion to the corresponding dimethylamino derivatives; there is a sharp deviation of the boiling point, surface tension and viscosity in the series of isoperiodic compounds from the straight line expressing the values of the constants as a function of the dipole moment (Figs. 1, 3, and 4).

EXPERIMENTAL

The methoxyphenols and dimethoxybenzenes were prepared by methylation of the respective hydroxy compounds with methyl iodide [14]. The anisidines were prepared by reduction of the corresponding methoxynitrobenzenes with zinc dust and HCl in alcoholic solution [15]. p-Anisidine was purified by recrystallization from water; pyrocatechol and resorcinol were purified by recrystallization from benzene; the remaining compounds were purified by three vacuum distillations.

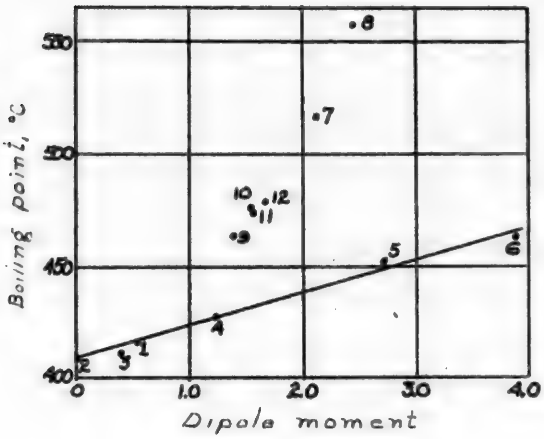


Fig. 2. 1) $C_6H_4(CH_3)_2$-o; 2) $C_6H_4(CH_3)_2$-p; 3) $C_6H_4(CH_3)_2$-m; 4) $C_6H_5OCH_3$; 5) C_6H_5CHO; 6) C_6H_5CN; 7) $C_6H_4(OH)_2$-o; 8) $C_6H_4(OH)_2$-p; 9) $C_6H_4(OH)CH_3$-o; 10) $C_6H_4(OH)CH_3$-m; 11) $C_6H_4(OH)CH_3$-p; 12) $C_6H_5CH_2OH$.

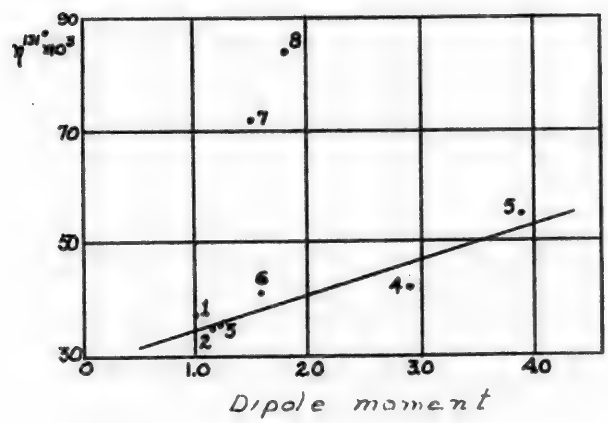


Fig. 3. 1) $C_6H_4(OCH_3)CH_3$-o; 2) $C_6H_4(OCH_3)CH_3$-m; 3) $C_6H_4(OCH_3)CH_3$-p; 4) $C_6H_5COCH_3$; 5) $C_6H_5NO_2$; 6) $C_6H_5N(CH_3)_2$; 7) $C_6H_4(NH_2)OCH_3$-o; 8) $C_6H_4(NH_2)OCH_3$-p.

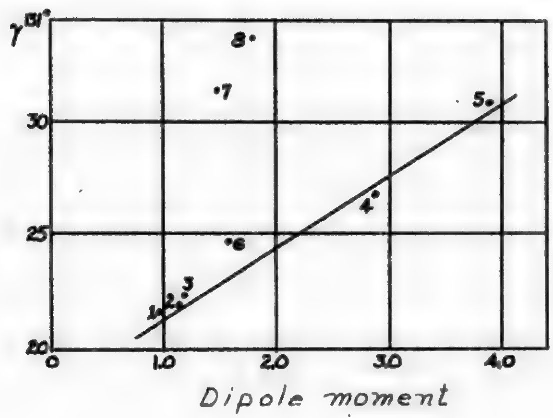


Fig. 4. 1) $C_6H_4(OCH_3)CH_3$-o; 2) $C_6H_4(OCH_3)CH_3$-m; 3) $C_6H_4(OCH_3)CH_3$-p; 4) $C_6H_5COCH_3$; 5) $C_6H_5NO_2$; 6) $C_6H_5N(CH_3)_2$; 7) $C_6H_4(NH_2)OCH_3$-o; 8) $C_6H_4(NH_2)OCH_3$-p.

The procedures for determination of density, viscosity and surface tension have been described previously.

All determinations were carried out in a steam thermostat [16]. The values of the constants of the hydroxy- and methoxy-substituted benzenes were generally in good agreement with the literature data [8, 17]. The values of the surface tension of pyrocatechol, resorcinol, p-methoxyphenol and m-anisidine are here given for the first time.

SUMMARY

1. Guaiacol in the liquid state possesses an intramolecular hydrogen bond, pyrocatechol in the liquid state is a mixed-associated compound, i.e., it is both inter- and intramolecularly associated.

2. o-Anisidine at 131° does not form an intramolecular hydrogen bond and resembles its isomers in being intermolecularly associated.

3. Densities, viscosities and surface tensions of a series of substituted phenols and anisoles at 131 and 184° were determined.

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THE DIBROMIDES OF BUTADIENE AND ITS HOMOLOGS

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In the preceding communication [1] it was shown that in the Raman spectrum of the butadiene dibromide with m.p. 53°, the double bond is represented by the frequency of 1655 cm^{-1}, and on this was based the assumption that this dibromide had a cis-configuration.

In the present investigation a study was made of the Raman spectra of the dibromides of a series of conjugated dienes. In Table 1 are set forth for comparison the frequencies of the C=C bond of the dibromides of butadiene, piperylene, bipropenyl (2,4-hexadiene), isoprene and diisopropenyl (i.e., 2,3-dimethyl-1,3-butadiene).

TABLE 1

Structure of dibromide	C=C frequency (in cm^{-1})
$CH_2Br-CH=CH-CH_2Br$	1655
$CH_2Br-CH=CH-CHBr-CH_3$	1657
$CH_3CHBr-CH=CH-CHBr-CH_3$	1659
$CH_2Br-CH=\underset{\displaystyle CH_3}{\underset{\vert}{C}}-CH_2Br$	1655
$CH_2Br-\underset{\displaystyle CH_3}{\underset{\vert}{C}}=\underset{\displaystyle CH_3}{\underset{\vert}{C}}-CH_2Br$	1650

TABLE 2

Substance	C=C frequency (in cm^{-1})
$CH_2Br-CH=CH-CH_2Br$	1655
$C_2H_5OCH_2-CH=CH-CH_2OC_2H_5$	1677
$CH_3COOCH_2-CH=CH-CH_2OCOCH_3$	1677

The dibromides of butadiene, piperylene and 2,4-hexadiene are disubstituted ethylenes. It was to be expected that their double bond would be characterized by a frequency of 1655-1660 cm^{-1} for the cis-form and by 1670-1680 cm^{-1} for the trans form. Isoprene dibromide is a trisubstituted olefin while 2,3-dimethyl-1,3-butadiene dibromide is a tetrasubstituted olefin. Their double bond should have the frequency of 1675-1680 cm^{-1}. Actually, however, the C=C bond of isoprene dibromide has the value of 1655 cm^{-1}, and 2,3-dimethyl-1,3-butadiene dibromide has 1650 cm^{-1}, i.e., there is a 20-25 cm^{-1} depression of the frequency of the double bond. This depression may be associated with the presence of two bromine atoms in the β-position to the double bond.

A slight depression of the frequency of the C=C bond by the bromine atom in the β-position has been noted in the literature [2]. Thus, in propylene the frequency of the C=C bond is 1648 cm^{-1}, whereas in allyl bromide it is 1638 cm^{-1}.

From the Raman spectrographic data, we can conclude that the addition of bromine to butadiene and its homologs proceeds according to a general mechanism.

On the basis of our observation of the lowering of the frequency of the C=C bond under the influence of two symmetrically arranged bromine atoms in the β-position to the double bond by 20-25 cm^{-1}, it may be assumed that in the dibromides of butadiene, piperylene and 2,4-hexadiene, the frequency of the C=C bond should be characterized by values of 1650-1660 cm^{-1} for the trans-isomers and of 1630-1640 cm^{-1} for cis-isomers. Consequently, our original conclusions about the configuration of the butadiene dibromides require greater precision. In order to check these conclusions, butadiene dibromide was converted by treatment with sodium ethoxide into 2-butene-1,4-diol diethyl ether [3], and by the action of sodium acetate in acetic anhydride into the diacetate of the same glycol [4]. In Table 2 are set forth for comparison the frequencies of the C=C bond of the dibromide of butadiene and of the ethers prepared from it.

Both the diethyl ether and the diacetate of butenediol are characterized by a C=C frequency of 1677 cm^{-1}, i.e., both compounds have a trans-configuration. Assuming that substitution of bromine by ether or ester groups should not be accompanied by a change of configuration, a trans-configuration must also be assumed for the original butadiene dibromide.

These data are in harmony with recently published results of an investigation of butadiene dibromide [5], which established that the infra-red spectrum contains an absorption maximum at 10.3μ, which is characteristic of trans-isomers. Lithium aluminum hydride reduces the dibromide to 2-butene, which by treatment with bromine is

converted into meso-2,3-dibromobutane. The dipole moment of butadiene dibromide (1.63 D) was found to be closer to the dipole moment of trans-1,4-dibromo-2,3-dimethyl-2-butene (1.72 D) than to the dipole moment of the cis-isomers of the latter (2.49 D).

Bromination of 2,3-dimethyl-1,3-butadiene gives a mixture of two products, one of which is a liquid and the other crystalline. The first of these is unstable and partly changes into the crystalline form even after standing for a short period. Close examination revealed that both are 1,4-dibromo-2,3-dimethyl-2-butene. The trans-configuration was assigned to the crystalline form and the cis- to the liquid. We have isolated both of the dibromides of 2,3-dimethyl-1,3-butadiene. The C=C bond frequency of the liquid isomer was 1650 $\pm$ 4 cm^{-1}, and that of the crystalline isomer 1650 $\pm$ 2 cm^{-1}. Consequently, it is impossible to distinguish spectrographically between the cis- and trans-forms of tetrasubstituted ethylene.

We give below the Raman spectra of the products that we studied.

1,4-Dibromo-2-butene. M.p. 53° (spectrum plotted in CCl_4 solution). We give the frequencies of the most intense lines after deducting the CCl_4 frequencies.

$\Delta\nu$: 171 (2), 442 (2), 593 (5), 628 (5), 1177 (5), 1206 (6), 1300 (1), 1655 (10).

1,4-Dibromo-2-pentene. B.p. 52.5° at 2 mm, d_4^{20} 1.7313, n_D^{20} 1.5466. Found %: Br 69.39. $C_5H_8Br_2$. Calculated %: Br 70.17.

$\Delta\nu$: 186 (6), 233 (1), 305 (5), 422 (3), 503 (2), 533 (3), 593 (4 b), 623 (4), 663 (10 b), 801 (4), 923 (2), 976 (1), 1010 (3), 1049 (2), 1110 (2), 1167 (2), 1201 (3), 1229 (3), 1314 (2), 1361 (2), 1388 (1), 1657 (10).

2,5-Dibromo-3-hexene. B.p. 66.5° at 2 mm, d_4^{20} 1.6216, n_D^{20} 1.5355. Found %: Br 66.15. $C_6H_{10}Br_2$. Calculated %: Br 66.11.

$\Delta\nu$: 305 (3), 593 (2 b), 623 (2), 668 (2), 845 (3), 899 (2), 938 (1), 1063 (3), 1154 (4), 1186 (5), 1210 (3), 1309 (2), 1659 (10).

1,4-Dibromo-2-methyl-2-butene. B.p. 70.5° at 2 mm d_4^{20} 1.7743. n_D^{20} 1.5620.

$\Delta\nu$: 223 (4), 330 (2), 386 (2), 437 (5), 448 (2), 583 (5 b), 618 (6 b), 648 (4), 777 (6), 850 (2), 909 (1), 1000 (2), 1063 (3), 1150 (5), 1206 (8), 1239 (6), 1328 (1), 1393 (1), 1435 (1), 1458 (1), 1655 (10).

1,4-Dibromo-2,3-dimethyl-2-butene. a) Crystalline form. M.p. 47° (spectrum taken in CCl_4 solution).

$\Delta\nu$: 295 (5), 402 (1), 518 (3), 563 (2), 618 (2), 643 (4), 688 (2), 723 (3), 855 (3), 1650 (8).

b) Liquid form. B.p. 75° at 4 mm, d_4^{20} 1.5504, n_D^{20} 1.4988.

$\Delta\nu$: 171 (3), 212 (2), 319 (2), 458 (5), 488 (7), 518 (9), 583 (4 b), 613 (5), 638 (10 b), 653 (4), 718 (5), 752 (4), 835 (1), 865 (1), 918 (3), 1000 (3 b), 1111 (3), 1177 (1), 1210 (10), 1285 (8), 1384 (1), 1449 (2), 1591 (1), 1650 (10).

Diethyl ether of 2-butene-1,4-diol [3]. B.p. 169-170°, d_4^{20} 0.8717, n_D^{20} 1.4246, MR_D 42.26, calculated, 41.96. Found %: C 66.78; H 11.30. $C_8H_{16}O_2$. Calculated %: C 66.63; H 11.18.

$\Delta\nu$: 850 (2), 870 (1), 1015 (1), 1101 (2), 1153 (1), 1290 (1), 1346 (1), 1398 (1), 1486 (3), 1677 (5).

2-Butene-1,4-diol diacetate [4]. B.p. 135-136° at 10 mm, d_4^{20} 1.0858, n_D^{20} 1.1062, MR_D 42.05, calculated 41.98. Found %: C 55.68; H 7.11. $C_8H_{12}O_4$. Calculated %: C 55.8; H 7.03.

$\Delta\nu$: 171 (2), 310 (1), 377 (1), 432 (1), 638 (4), 835 (3), 879 (1), 967 (2), 1030 (3), 1177 (2), 1229 (2), 1266 (1), 1290 (2), 1309 (1), 1356 (1), 1384 (1), 1435 (2), 1458 (2), 1677 (10), 1736 (5).

SUMMARY

A study of the Raman spectra of the dibromides of butadiene and its nearest homologs, as well as of the diethyl ether and diacetate of 2-butene-1,4-diol, showed that the addition of bromine to these conjugated dienes proceeds according to a common mechanism. The 1,4-dibromides formed possess a trans-configuration.

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THE PROCESS OF FORMATION OF POLYAMIDE RESINS

IV. THE STEPWISE CHARACTER OF THE PROCESS OF FORMATION OF POLYAMIDE RESINS AND OF THE PRODUCTS OF REACTION OF ε-CAPROLACTAM WITH ADIPIC ACID

A. S. Shpitalnyi, K. E. Perepelkin and E. A. Meos

Although at the present day, the formation of polyamides is believed to be a stepwise process [1], papers have been published which attribute a radical character instead of a stepwise character to the formation of polyamides if the starting material is ε-caprolactam [2].

We have presented some evidence for the stepwise character of the transformation of ε-caprolactam into polymer [3,4]. For example, the products of reaction of ε-caprolactam with some dicarboxylic acids or amines were isolated, also low-molecular polymers which were intermediate products of the transformation of ε-caprolactam into high-molecular polyamides. The previously described products of reaction were obtained with an equimolecular ratio of components. Since we assumed that the isolation of low-molecular products with a larger number of links than in the preceding investigation is further evidence of the stepwise character of the formation of polyamides from ε-caprolactam, we made an attempt to obtain products of interaction with a molar ratio of starting components – adipic acid and ε-caprolactam – of 1:2 and 1:4. In this case we expected to obtain the compounds:

$$HOOC-(CH_2)_5-NH-CO(CH_2)_4-CO-NH-(CH_2)_5-COOH; \qquad (I)$$

$$HO-(CO(CH_2)_5-NH)_2-CO-(CH_2)_4-CO-(NH-(CH_2)_5-CO)_2-OH. \qquad (II)$$

The composition of these compounds was established by analysis of their silver salts.

A comparison of the properties of the silver salts of the products of reaction of ε-caprolactam with adipic acid with those of salts of adipic and other dicarboxylic acids established that some of their properties differ; in particular they differ in their solubility in water.

Solubility in Water of Silver Salts of some Dicarboxylic Acids

Prep. no.	Salt	Temp. (in °)	Solubility (in g per 100 g water)	Literature reference
1	Silver oxalate	18	0.034	[5]
2	Silver succinate	18	0.0176	[6]
3	Silver adipate	14	0.0166	[7]
4	The same	100	0.049	[7]
5	Silver salt of product of reaction of adipic acid with ε-caprolactam in equimolar ratio	17	0.082	–
6	The same	100	0.46	–

Since the silver salt of the product of reaction of ε-caprolactam with adipic acid was found to have a fairly high solubility, wahhing of the salts was effected in succession with small portions of water, alcohol and ether.

The external appearance of the products changed in dependence on the length of their molecules. Products of interaction whose molecules consist of two or three links have a waxy appearance. Products with four links in the molecule resemble a hard resin and have a conchoidal fracture. Analysis of the silver salts of these products showed that the adipic acid enters completely into reaction with ε-caprolactam, since it was not detected in the reaction products.

When the adipic acid was replaced by benzoic acid, part of the latter did not enter into reaction even with a considerable excess of ε-caprolactam. This interesting observation was made by A. Matthes [2] and confirmed by our experiments. Matthes explained this phenomenon by the susceptibility of the benzoic acid – ε-caprolactam reaction product to decomposition during the reaction with formation of radicals of ε-caprolactam.

If this interpretation were correct, then the phenomenon should also be observed in the reaction of adipic acid with ϵ-caprolactam, but this is not the case.

Considering that the boiling point of adipic acid is 265° (at 100 mm) [8], whereas benzoic acid can sublime at as low as 100° [9], and that the reaction temperature is 240°, there can be no doubt at all that in the reaction of benzoic acid with ϵ-caprolactam, a part of the benzoic acid will be outside the sphere of reaction. This must be the actual reason why benzoic acid is found in the cooled reaction mass even with an excess of the ϵ-caprolactam reacting with it.

Consequently, the experimental material of the present investigation, likewise confirms the stepwise character of the transformation of ϵ-caprolactam into polyamide.

EXPERIMENTAL

Reaction of ϵ-Caprolactam with Adipic Acid in Equimolecular Ratio and Properties of the Final Product

The product of interaction of adipic acid with ϵ-caprolactam in equimolecular ratio was prepared as previously described [3]. It forms a grey melt with a waxy appearance and consistency, soluble in water on heating, slightly soluble in alcohol, insoluble in ether and benzene.

The silver salt of the product is prepared in the following manner. The melt is dissolved in water with heating and treated with excess of calcium carbonate until carbon dioxide ceases to come off. The solution is filtered and to the filtrate is added an excess of 5-8% solution of silver nitrate. The white flocculent precipitate is collected, washed with a little water and then with alcohol (until it gives a negative test for calcium with alcoholic oxalic acid) and dried after washing with ether. Analysis was carried out by the usual procedure [10].

0.2795 g sub.: 0.1690 g AgCl. 0.2800 g sub.: 0.1703 g AgCl. Found %: Ag 45.53, 45.77. $C_{12}H_{19}O_5NAg_2$. Calculated %: Ag 45.61.

The solubility of the silver salt of the product of reaction in 100 g water at 17° is 0.082 g; at 100°, it is 0.46 g.

Reaction of ϵ-Caprolactam with Adipic Acid in 2:1 Molar Ratio and the Properties of the Product

The product of interaction and its silver salt were prepared by the above procedure. The outward appearance of the melt and its properties were the same as those of the product of equimolar amounts of the components.

Reaction of ϵ-Caprolactam with Adipic Acid in 4:1 Molar Ratio and the Properties of the Product

0.7307 g adipic acid and 2.2632 g ϵ-caprolactam in a sealed tube (from which the air had been purged with carbon dioxide) were heated at 240° for 25 hours. The white melt was a hard resin (conchoidal fracture), poorly soluble in water even when boiled, insoluble in alcohol, ether and benzene.

The silver salt of the reaction product was prepared and analyzed as before (when dissolved by addition of nitric acid, the dicarboxylic acid — the product of reaction of ϵ-caprolactam with adipic acid — does not dissolve and must be filtered off).

0.2532 g sub.: 0.0888 g AgCl. 0.2662 g sub.: 0.0950 g AgCl. Found %: Ag 26.39, 26.86. $C_{30}H_{52}O_8N_4Ag_2$. Calculated %: Ag 26.56.

The reaction product, therefore, has formula (II).

Reaction of ϵ-Caprolactam with Benzoic Acid in 1:1 Molar Ratio

2.442 g benzoic acid and 2.2632 g ϵ-caprolactam (equimolar ratio) were heated in an ampoule, from which the air had previously been displaced by carbon dioxide, for 46 hours at 240°. Part of the unreacted benzoic acid adhered to the walls of the ampoule. The product had a soft, waxy consistency.

0.3118 g sub.: 0.1033 g AgCl. 0.3100 g sub.: 0.1030 g AgCl. Found %: Ag 24.93, 25.01. Calculated %: Ag for products of interaction of ϵ-caprolactam with benzoic acid (in 1:1 molar ratio) 33.48; (in molar ratio of 2:1) 24.78.

Consequently, only a portion of the benzoic acid had reacted with caprolactam. In order to establish whether the reaction mass contains benzoic acid, 1.9170 g of the latter was extracted with ether. Weight of

extract was 0.9794 g (51.2%). It had a waxy consistency. The residue after extraction (0.9334 g or 48.7%) formed hard pellets.

The product obtained after evaporation of the ethereal extract was titrated with 0.1 N NaOH solution in presence of phenolphthalein.

0.0693 g sub.: 3.95 ml 0.1 N NaOH. 0.0700 g sub.: 3.96 ml 0.1 N NaOH.

Calculated on benzoic acid the ethereal extract contains 70.5, 70.0%, while calculated on benzoylaminocaproic acid it contains 135.8, 135.0%. Consequently, the portion extracted consists of benzoic acid (34.2%) and benzoylaminocaproic acid (65.8%). ε-Caprolactam is absent from the portion extracted because it is capable of being completely converted to calcium salt (after treatment of the aqueous solution of the extracted portion with calcium carbonate, filtration and drying, a product is obtained which is completely insoluble in ether).

Reaction of ε-Caprolactam with Benzoic Acid in 2:1 Molar Ratio

The product of reaction of ε-caprolactam with benzoic acid in 2:1 molar ratio and its silver salt were prepared as in the preceding case. The silver salt is a white powder.

0.1455 g sub.: 0.0446 g AgCl. 0.1500 g sub.: 0.0453 g AgCl. Found %: Ag 23.07, 22.73. Calculated %: Ag for products of reaction of ε-caprolactam with benzoic acid (in 2:1 molar ratio) 24.78; (in 3:1 molar ratio) 19.66.

It follows from the analytical data that in this case also, not all the benzoic acid had entered into reaction with the caprolactam.

SUMMARY

1. Isolation of the products of interaction of adipic acid with ε-caprolactam in 1:2 and 1:4 molar ratios yielded supplementary evidence for the stepwise-polymerization process during the formation of a polyamide from ε-caprolactam.

2. A description is given of some of the properties of the products of reaction of adipic acid with ε-caprolactam in various molar ratios; determinations were made of the solubility of the silver salt of the product of reaction of equimolar amounts of the starting components.

3. It was shown that the presence of benzoic acid in the reaction mixture after interaction of the former with excess of ε-caprolactam is due to the low temperature of sublimation of benzoic acid.

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* See Consultants Bureau Translation, page 1311.

** See Consultants Bureau Translation, page 1447.

ACYLATION OF THE ENOL FORM OF ACETALDEHYDE

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A number of transformations of acetaldehyde can proceed with participation of vinyl alcohol as the reactive form of acetaldehyde. An example of such a transformation is evidently the reaction of acetaldehyde with acetic anhydride [1-3] $CH_3-CHO \rightarrow CH_3CH(OCOCH_3)_2 \rightarrow CH_2=CH-OCOCH_3$.

The reaction between acetaldehyde and acetic anhydride, leading to formation of ethylidene diacetate, has found practical application in the production of vinyl acetate [4]. For this purpose ethylidene diacetate is subjected to thermal decomposition. It is found that in this reaction, the acetaldehyde can be successfully replaced by paraldehyde.

Reactions of the same class are the formation of ethylidene diacetate by heating acetyl chloride with acetaldehyde [5], the formation of phenylvinyl acetate [6] and α-chloro- and α-bromovinyl acetates [7] from the respective aldehydes and acetic anhydride.

Acetaldehyde has been observed to form a compound $(H_2C=CHO)_2Hg \cdot HgO$ [8] and mercuric chloride in aqueous potassium carbonate solution; the yield of this mercury compound was found to be directly proportional to the concentration of alkali in the solution [9].

Nesmeyanov and Lutsenko [10] obtained chloromercuriacetaldehyde when starting from vinyl ethers. Treatment of this compound with acetyl chloride or benzoyl chloride in xylene readily leads to vinyl benzoate:

$$ClHgCH_2CHO + RCOCl \rightarrow CH_2=CH-O-COR + HgCl_2.$$

Enol acetates of acetaldehyde, phenylacetaldehyde, isobutyraldehyde and enanthal [11] have also been obtained by heating these aldehydes with acetic anhydride in presence of potassium acetate.

Acetylation of acetaldehyde, paraldehyde, butyraldehyde and isobutyraldehyde with isopropenyl acetate [12] also yielded the enol acetates. The yield of vinyl acetate here was 78% when starting from acetaldehyde and 88% of the theoretical when starting from paraldehyde.

Some catalytic processes with acetaldehyde as catalyst, for example the hydration of dicyanogen to oxamide [13], pass through the stage of formation of vinyl alcohol.

Methods are described in the literature for preparation of a series of perfectly stable α-substituted vinyl alcohols not susceptible to transition to the keto form [14], for example 2-mesityl-2-phenylvinyl, 2-duryl-2-phenyl-, 2-(3-bromomesityl)-2-phenyl- and 2,2-(2,4,6-triisopropylphenyl)-vinyl alcohols.

X-ray crystallographic investigations showed that the stability of these vinyl alcohols is due to the spatial arrangement of the groups which hinder rearrangement to the keto form.

On the basis of an analysis of the above-cited literature data we concluded that it was entirely probable that any desired vinyl esters could be obtained from acetaldehyde in presence of enolizing substances.

The reaction was performed in a medium of organic tertiary bases (pyridine, quinoline and dimethylaniline) with acetaldehyde and certain other aldehydes. Anhydrides and acid chlorides were tried out as enolizing media. Similar experiments were also run with paraldehyde.

The principal constants of the prepared vinyl esters were determined; in some cases also the iodine numbers and the saponification numbers. Esters containing a large number of double bonds were analyzed by ozonization.

Acylation of acetaldehyde with anhydrides gives low yields of vinyl esters. When using anhydrides of higher acids, the formation of vinyl esters was not generally observed. Acylation of the enol form of acetaldehyde with acid chlorides in all cases led to vinyl esters in high yields.

The best results were had when pyridine was the reaction medium. Quinoline reacts very violently with the acid chlorides and in some cases causes resinification of the acetaldehyde. Dimethylaniline has no advantage over pyridine and in some cases hinders the separation of the vinyl esters in the pure state.

EXPERIMENTAL

The first series of experiments was performed with acetaldehyde and various anhydrides. The anhydride was gradually added to a mixture of acetaldehyde and anhydrous quinoline, pyridine or dimethylaniline with continuous stirring and cooling with iced water; after the whole of the anhydride had been added, the mixture was heated to 60-80° under reflux with iced water cooling. The reaction products were then poured into water, separated in a separating funnel and repeatedly washed by shaking with water. After drying over anhydrous sodium sulfate, the product was fractionated (if necessary in vacuum).

The results of this part of the investigation are set forth in Table 1.

TABLE 1

Acylation with Anhydrides

Anhydride	Medium	Yield of ester (in % of theoretical)	
		with acetaldehyde	with paraldehyde
Acetic	Quinoline	36	20
	Dimethylaniline	24	–
	Pyridine	20	–
Propionic	Quinoline	29	22
	Dimethylaniline	27	–
	Pyridine	16.5	–
Butyric	Quinoline	25	16
	Dimethylaniline	32	–
	Pyridine	14	–
Stearic	Quinoline	0	–

All the experiments listed in the table were carried out with molar ratios of anhydride to acetaldehyde and to the amines of 1:0.5:3. A few experiments showed that these ratios are the optimum for maximum yields of esters.

Stearic anhydride did not react either in the above conditions or in any of their variations. In no case was the formation of ethylidene glycol esters observed.

A second series of experiments was performed with acetaldehyde, paraldehyde and acid chlorides in a medium of dimethylaniline, pyridine and quinoline.

To a mixture of acetaldehyde or paraldehyde with quinoline, dimethylaniline or pyridine, cooled with iced water or snow-salt mixture, was gradually added the acid chloride with stirring. The reaction mixture was afterwards slowly heated to 50-60° and then poured into water or onto ice; the ester layer was separated, dried over anhydrous sodium sulfate and fractionated (sometimes in vacuum).

Molar ratios: 2 moles acetaldehyde were reacted with 1 mole chloride of a mono-basic acid or 0.5 mole chloride of a dibasic acid in presence of 3-5 moles of base.

Results are set forth in Table 2.

TABLE 2

Acylation with Chloroanhydrides

Acid chloride	Medium	Yield of ester (in % of theoretical)	
		with acetaldehyde	with paraldehyde
Acetyl chloride	Quinoline	40.5	28.0
Stearyl chloride	Quinoline	92.0	65.0
Acetyl chloride	Dimethylaniline	89.0	–
Stearyl chloride	Dimethylaniline	62.0	–
Acetyl chloride	Pyridine	86.0	85.0
Stearyl chloride	Pyridine	88.0	68.0

The results obtained justify the conclusion that our method is applicable to the synthesis of vinyl esters. We carried out the reaction with 29 substances and obtained in all cases the corresponding vinyl esters.

Table 3 contains the constants and yields of esters prepared by this method. The yields of vinyl esters enumerated in the table were obtained when using pyridine as the reaction medium (with acetaldehyde). When using quinoline, the yields of esters of higher fatty acids were slightly increased but those of esters of lower aliphatic acids were considerably reduced. Replacement of acetaldehyde by paraldehyde in all cases lowered the yield of vinyl esters.

TABLE 3

Acylation with Acid Chlorides

Acid chloride	Yield of ester (in % of theor.)	B.p. (in °) (pressure in mm) found	B.p. literature data	d_4^{20} found	d_4^{20} literature data	n_D^{20} found	n_D^{20} literature data
Acetyl	82	72-73 (760)	73 (760) [15]	0.9321	0.9342 [15]	1.3958	1.3958 [15]
Valeryl	78	134 (760)	133-134 (760) [16]	0.9080	–	1.4170	–
Caproyl	77	162 (760)	165-170 (760) [16]	0.8832	0.8837 (30°) [17]	1.4160	1.4152 (30°) [17]
Enanthyl	79	182-183 (760)	–	0.8992	–	1.4206	–
Capryl	78	90 (10)	94 (13) [16]	0.8889	0.889 [18]	1.4260	1.4271 [18]
Pelargonyl	82	130 (42)	133-133.5 (50) [17]	0.8690	0.8689 (30°) [17]	1.4289	1.4291 (30°) [17]
Caprinyl	80	119-120 (10)	148 (50) [17]	0.8681	0.8670 (30°) [17]	1.4329	1.4320 (30°) [17]
Undecyl	82	124-125 (8)	125 (10) [19]	0.8820	–	1.4355	–
Lauryl	86	123-124 (4)	123 (4) [16]	0.8641	0.8770 [18]	1.4371	1.4386 [18]
Myristyl	88	152 (3)	150 (3) [16]	0.8620	0.8617 (30°) [17]	1.4412	1.4407 (30°) [17]
Palmityl	79	162 (2)	165 (2) [16]	0.8612	0.8602 (30°) [17]	1.4441	1.4438 (30°) [17]
Stearyl	88	166-167 (2)	167 (2) [16]	0.8521 (30°)	0.8517 (30°) [17]	1.4426 (30°)	1.4423 (30°) [17]
Trimethylacetyl	86	113-114 (760)	110-112 (760) [18]	0.8820	0.873 [18]	1.4072	1.4068 [18]
Phenylacetyl	80	126-128 (32)	88-90 (4) [16]	1.0271	–	1.5002	–
α-Chlorobutyryl	82	157-158 (760)	–	1.0610	–	–	–
β-Chlorobutyryl	80	163-164 (760)	–	1.0581	–	1.4260	–
γ-Chlorobutyryl	80	179-180 (760)	–	1.0702	–	1.4486	–
Bromoacetyl	51	76 (40)	–	1.5058	–	1.5556	–
Iodoacetyl	34	72-73 (20)	–	1.8101	–	1.4844	–
Methacryl	75	111-112 (760)	–	1.4029	–	–	–
Undecenyl	75	127 (10)	–	0.8780	–	1.4462 (25°)	–
Oleyl	68	172-173 (2)	173 (2) [16]	0.8699	0.869 [18]	1.4538	1.4533 [18]
Adipyl	54	125-126 (12)	110-124 (10) [19]	–	–	–	–
Sebacyl	62	142 (3)	–	–	–	–	–
Fumaryl	38	138 (1)	–	–	–	–	–
Maleyl	35	94 (10)	–	–	–	–	–
Benzoyl	89	75 (4)	72-74 (3) [16]	–	1.0706 [18]	–	1.5259 [18]
o-Phthalyl	66	138-139 (5)	–	–	–	–	–
β-Naphthoyl	68	142-143 (2)	153 (4) [16]	–	–	–	–

A small amount (up to 1%) copper resinate was added to the vinyl esters prior to distillation to inhibit polymerization.

Reactions between butyraldehyde and enanthal and acetyl chloride in a pyridine medium were performed in exactly the same manner. The enol acetate of butyraldehyde was obtained in a yield of 78.5% of the theoretical and had b.p. 129-130°; the enolacetate of enanthal was obtained in 52% yield and had b.p. 88-89° at 17 mm.

It should be pointed out that the pyridine, quinoline, dimethylaniline and acetaldehyde used in the reactions must be thoroughly dried, since even traces of moisture in the starting materials considerably reduce the yield of vinyl ester. Freshly distilled reagents are also desirable.

SUMMARY

1. The results of our present investigation confirm that acetaldehyde reacts in its tautomeric form (vinyl alcohol) in presence of enolizing substances.

2. For the first time, the vinyl esters of the following acids were prepared: enanthic, undecyl, α-, β-, and γ-chlorobutyric, bromoacetic, iodoacetic, methacrylic, undecylenic, sebacic, fumaric, maleic and o-phthalic.

3. The method was extended to the preparation of enol acetates of other aldehydes.

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THE ROLE OF THE OXIDATION-REDUCTION PROPERTIES OF α-HYDROXY KETONES IN INITIATED POLYMERIZATION*

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Intermolecular and intramolecular oxidation-reduction reactions [1], previously designated as simultaneous oxidation-reduction reactions [2], are characterized by migration of oxygen within a molecule without change of composition or between different molecules, for example, in the removal or addition of oxygen-containing molecules (water, alcohol, etc.), as was discussed in previous papers [1, 3].

Hydroxyaldehydes and hydroxyketones, for which intramolecular oxidation-reduction, hydroxyketonic and acidic transformations are known, are characterized by great ease of oxidation of alcoholic groups (formation of aldehydoketones and diketones), and also by reduction of their carbonyl groups to alcohol groups with transformation into glycols. Danilov and Venus-Danilova [4] have studied the oxidation of a ketone-alcohol to a diketone and reduction of the latter to ketoalcohol.

For the understanding of the hydroxyketonic and acidic transformation of α-hydroxyaldehydes and α-hydroxyketones, great interest attaches to the characterization of hydroxycarbonyl compounds in respect of the oxidizability of their alcohol group and of the reducibility of the carbonyl group with reference to ease of cleavage of hydrogen atoms from the alcohol groups and capture of the detached hydrogen atoms by the carbonyl groups. The susceptibility to reduction of carbonyl groups can be evaluated from polarographic data [5].

At the present time extensive use is made at home and abroad of oxidation-reduction systems in the initiation of polymerization of unsaturated compounds. The action of a peroxide (initiator) in polymerization is intensified by introducing into the medium a substance which is readily oxidized and reduced, for example, benzoin and other hydroxycarbonyl compounds (in Kern's experiments [6]) and a polyvalent metal ion, for example, iron salts of organic acids which influence the decomposition of peroxide.

With the objective of evaluating the oxidation-reduction properties of ketoalcohols with primary and secondary alcohol groups and in dependence on the radicals, we studied the kinetics of polymerization of styrene in an oxidation-reduction system with participation of two isomeric ketoalcohols – propionylcarbinol and methylacetylcarbinol; benzoin was used for comparison. The great activity of 1,3-dihydroxy-2-propanone benzoin reducing substance was confirmed by I. Kolthoff in the copolymerization of butadiene and styrene [7]. The extent of polymerization is conveniently measured by the dilatometric method as applied by B.A. Dogadkin and co-workers [8].

Our experiments on the polymerization of styrene in presence of an oxidation-reduction system (benzoyl peroxide, iron naphthenate, ketoalcohol) led to the conclusion that of the three alcohols compared, the greatest activity is manifested by benzoin. The isomeric α-hydroxybutanones (methylacetylcarbinol and propionylcarbinol) were inferior to benzoin; they showed, however, considerable activity, although the primary ketoalcohol was less active than the secondary isomer (methylacetylcarbinol). It should be mentioned that polarographic experiments [5] revealed a lower susceptibility to reduction on the part of propionylcarbinol in comparison with methylacetylcarbinol, and the latter in turn had a lower susceptibility to reduction than benzoin. It might be thought that the susceptibility to oxidation to dicarbonyl compounds of these ketoalcohols also rises from propionylcarbinol to methylacetylcarbinol to benzoin, but this point is still under investigation. A good criterion of the oxidation-reduction properties of ketoalcohols must be their influence (in dependence on the structure) on the rate of polymerization when they are used in oxidation-reduction systems.

On the basis of the results obtained, we may conclude that the ketoalcohols under consideration may be arranged in the following order in respect of their activity in oxidation-reduction systems during polymerization:

benzoin > methylacetylcarbinol > propionylcarbinol.

Ketoalcohols which function as reducers in oxidation-reduction systems during polymerization are oxidized. Consequently the relative susceptibility to oxidation of the above ketoalcohols corresponds to a series

* This is the third communication in a series on "Hydrolytic and solvolytic intermolecular and intramolecular oxidation-reduction"; see Danilov, J. Gen. Chem., 18,200 (1948).

in which they are arranged in order of reductive ability as determined by polarographic measurements as previously described [5].

This concurrence in susceptibility to oxidation and reduction is probably not a general rule for all ketoalcohols, but it results in the case of our ketoalcohols in benzoin having increased susceptibility both to oxidation and reduction due to the presence in it of phenyl groups.

The comparison in this respect of propionylcarbinol and methylacetylcarbinol indicates that a primary alcoholic group weakens the oxidation-reduction properties of a molecule. Evidently the $COCH_2OH$ group is less susceptible to oxidation and reduction than the COCHOH group. These properties of ketoalcohols must evidently be correlated with the facts which indicate that α-hydroxybutyraldehyde isomerizes to methylacetylcarbinol whereas in the same conditions the isomerization of propionylcarbinol to methylacetylcarbinol is not observed.

EXPERIMENTAL

Experiments on polymerization of styrene were carried out at 50° in a block, using as the initiating system (as previously used by Kern [6]): benzoyl peroxide, iron (Fe^{+++}) naphthenate and ketoalcohol. A comparison was made between benzoin, methylacetylcarbinol (acetoin) and propionylcarbinol (1.25 %). An experiment was run in parallel without addition of ketoalcohol. The extent of polymerization was determined (as mentioned above) by the dilatometric method —contraction of volume of the system on transition from monomer to polymer.*

The starting substances were carefully purified. Before an experiment, the styrene which had been purified in the usual manner and dried, was distilled in vacuum in a current of nitrogen; b.p. 40° at 14 mm.

Benzoyl peroxide was recrystallized from chloroform with addition of methanol at room temperature; m.p. 104°.

The ketoalcohols were prepared and purified by the previously described methods [9, 10]. The following were used: Propionylcarbinol with b.p. 64° at 24 mm, n_D^{20} 1.4242 methylacetylcarbinol with b.p. 56° at 34 mm, n_D^{20} 1.4200; benzoin with m.p. 133°.

In a flask with three taps (Schmidlin-Schlenk type), ensuring complete exclusion of [11] from the liquid, was prepared a solution of styrene with addition of 1.25% benzoyl peroxide and 0.05% iron naphthenate. Quantities were 158 ml (142.2 g) styrene, 1.78 g benzoyl peroxide and 0.7 g iron naphthenate. The glass ampoules used had a graduated scale for measurement of contraction, two necks and a pouch for addition of the ketoalcohol. The volume of each ampoule was measured in advance upto a specified graduation mark. The ampoules were connected to a set of taps linked in turn to a vacuum pump and a nitrogen supply. The system was pumped out three times and purged with nitrogen between each pumping. The ampoules were filled, in countercurrent with nitrogen, with the prepared solution from the Schlenk apparatus, in each case up to a specific mark on the graduation. Into the pouches of the ampoule were also charged the calculated weights of ketoalcohols. One ampoule (control) was left without this addition. After the ampoules had been filled, their necks were sealed off while a stream of nitrogen was passed. Before immersion in the ultrathermostat, each ampoule was well shaken to enable the ketoalcohol to fall into the styrene solution. After keeping in the thermostat for 15 minutes, the level of the liquid in each ampoule was noted. Measurements were made every hour over a period of 20 hours. Curves of styrene polymerization velocity as a function of the ketoalcohol additions are plotted in the diagram, the abscissas of which are durations and the ordinates are % of polymerized styrene calculated from the formula [12]:

$$S = \frac{\Delta v_{obs.}}{\Delta v_{max}} \cdot 100$$

where S = percentage polymerization;

$\Delta v_{obs.}$ = observed contraction of volume (in ml);

Δv_{max} is calculated for each ampoule from the formula for styrene:

$$\Delta v_{max} = 16.6 \cdot v \text{ of ampoule.}$$

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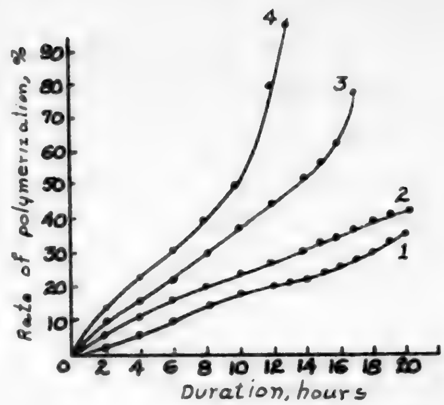
We see from the diagram that after 10 hours' heating the polymerization in the ampoule without addition of ketoalcohol had proceeded to the extent of 18%; with addition of propionylcarbinol it was 23%; with addition of methylacetylcarbinol it was 30%; and with addition of benzoin it was 50%. The most active of the three ketoalcohols was benzoin — a ketoalcohol containing phenyl radicals. Of the other two isomeric ketoalcohols, the first was less active than the second, although the addition of propionylcarbinol slightly accelerated polymerization in comparison with the control.

Further observations of the course of polymerization, with assumption of the suitability of the above formula, gave the following information: In the case of benzoin, after heating for 10 hours the rate of polymerization of styrene increased sharply; after 13 hours' heating the extent of polymerization, calculated from the above formula, reached nearly 100%. In the ampoule with addition of methylacetylcarbinol, after 14 hours heating the polymerization rate sharply increased and attained a 50% value, rising again after 17 hours to 73.5%. After 20 hours heating at 50° in the experiments without addition of ketoalcohol, polymerization proceeded to the extent of 36%, while with addition of propionylcarbinol it was 42%.



Curves of styrene polymerization velocities in presence of benzoyl peroxide (1.25%), iron naphthenate (0.05%) and ketoalcohol (1.25%). 1) Without addition of ketoalcohol; 2) with addition of propionylcarbinol; 3) with addition of methylacetylcarbinol; 4) with addition of benzoin.

Further observations were made at room temperature and revealed that in the experiments without addition of ketoalcohol the polymerization did not proceed any further; in those with addition of propionylcarbinol there was a slow decrease of volume which after 50 hours observation (after previously keeping for 20 hours at 50°) corresponded to 67% polymerization of the styrene. In the control experiment the polymerization after this period had proceeded to the extent of 38%.

SUMMARY

1. Participation of hydroxycarbonyl compounds in oxidation-reduction systems during polymerization of unsaturated compounds can serve as a measure of the oxidation-reduction properties.

2. Experiments on styrene polymerization were carried out with the help of an oxidation-reduction system consisting of 1.25% benzoyl peroxide, 0.05% iron (Fe^{+++}) naphthenate and 1.25% ketoalcohol (propionylcarbinol, methylacetylcarbinol, or benzoin).

The experiments showed that benzoin was the most active agent in styrene polymerization, followed in order by methylacetylcarbinol and propionylcarbinol.

3. The susceptibility to oxidation of the ketoalcohols, manifested in their participation in the oxidation-reduction system during styrene polymerization, is in harmony with data from experiments on determination of their susceptibility to reduction at the dropping mercury cathode.

4. The oxidation-reduction properties of propionylcarbinol and methylacetylcarbinol are consistent with the fact that propionylcarbinol does not isomerize to methylacetylcarbinol in the conditions in which the latter is formed from α-hydroxybutyraldehyde.

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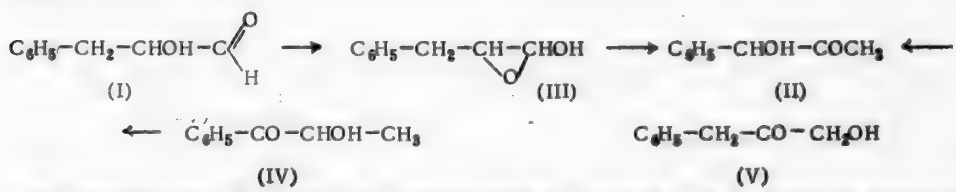
ISOMERIZATION OF α-HYDROXYALDEHYDES

XIII. TRANSFORMATIONS OF α-HALOGENO- AND α-HYDROXYKETONES WITH A PRIMARY ALCOHOLIC GROUP

S. N. Danilov and N.S. Tikhomirova-Sidorova

In papers by S.N. Danilov and E.D. Venus-Danilova it was shown by reference to a series of examples [1] that α-halogeno- and α-hydroxyaldehydes of the aliphatic and polymethylene series are transformed into α-hydroxyketones and isomeric acids (in analogy with the epimeric and saccharinic rearrangement of monoses) in conditions of acidic and alkaline-salt catalysis [2]. These rearrangements can be predicted (S.N. Danilov [1]) on the basis of isomeric transformations in the group of monoses [3] and dihalogenoketones [4], as well as according to A.E. Favorsky's alcoholic-oxide scheme proposed for interpretation of the acidic transformation of monohalogenoketones [5] and later (1928) for explanation of the isomerization of ketoalcohols [6].

Benzylglycolaldehyde (I) is isomerized [7] to a secondary ketoalcohol – phenylacetylcarbinol (II). The other isomeric ketoalcohol – methylbenzoylcarbinol (IV), was not isolated. It was known [6, 8] that methylbenzoylcarbinol isomerizes to phenylacetylcarbinol. More noteworthy, however, is the fact that benzylglycolaldehyde does not yield a ketoalcohol with a primary alcoholic group (V) which might have been formed in accordance with Favorsky's alcoholic-oxide scheme (III) and as the closest isomer of the hydroxyaldehyde:



The transformation of α-hydroxybutyraldehyde [9] also leads directly to 3-hydroxy-2-butanone which contains a secondary alcoholic group.

Similarly α-hydroxyenanthaldehyde forms a hydroxyketone with an acetyl group on rearrangement [10]. It was first suggested [7] that the ketoalcohol with a primary alcohol group is an intermediate product in the isomerization of α-hydroxyaldehydes (monosubstituted glycolaldehydes) to α-hydroxyketones and is transformed in the instant of formation into a ketoalcohol with a secondary alcohol group.

A few years ago the problem was posed [11] of synthesis of ketoalcohols containing a primary alcoholic group for the study of their possible role in the intermediate stage of isomerization of α-hydroxyaldehydes to ketoalcohols. In our previous paper [12] we described monochloroketones corresponding to methylethyl ketone, and we showed that 1-chloro-2-butanol may form, on hydrolysis of the chlorine, two isomeric ketoalcohols, i.e., rearrangement takes place to give an isomeric ketoalcohol with a secondary alcohol group. We have now supplemented the data in this field with the aim of establishing whether primary α-ketoalcohols are transformed into secondary in conditions similar to those of the hydroxyketonic rearrangement of α-hydroxyaldehydes. The possibility of isomerization of halogenoketones and their corresponding ketoalcohols with a primary alcohol group into saturated acids was also investigated.

An investigation was made of primary ketoalcohols 1-hydroxy-2-butanone $CH_3CH_2COCH_2OH$ and phenylacetol (V), the heating of which in presence of sulfuric acid was expected to lead to ketoalcohols with secondary alcoholic groups due to isomerization of α-hydroxybutyraldehyde and benzylglycolaldehyde. However, neither 3-hydroxy-2-butanone nor phenylacetylcarbinol was obtained in our conditions from ketoalcohols with a primary alcohol group. Evidently the transformation of α-hydroxyaldehydes into secondary α-ketoalcohols does not proceed through the stage of a primary ketoalcohol.

In our experiments two ketoalcohols – 1-hydroxy-2-butanone and the isomeric 3-hydroxy-2-butanone (VIII), were obtained from chloromethylethyl ketone (1-chloro-2-butanone) (VI) and 1-hydroxy-2-butanone (VII) respectively, as reported previously [12], on heating in an alkaline or aqueous medium with salts of lead or silver:

$$CH_3-CH_2-CO-CH_2Cl \xrightarrow[PbO,KOH]{100^\circ} CH_3-CH_2-CO-CH_2OH + CH_3-CHOH-CO-CH_3$$

(VI) (VII) (VIII)

The presence of the secondary ketoalcohol (VIII) was proved by isolation of its dimer (2, 3-butanedione) on oxidation, and by the preparation of its semicarbazone, phenylosazone, p-nitrophenylhydrazone and 2,4-dinitrophenylhydrazone.

The yield of 3-hydroxy-2-butanone is increased by choosing more drastic conditions of hydrolysis of 1-chloro-2-butanone. This indicates the possibility of isomerization of 1-hydroxy-2-butanone into 3-hydroxy-2-butanone, but suitable conditions of isomerization were not found. If such a transformation is indeed possible, then it evidently takes place in special conditions.

When using 7% alkali and lead hydroxide, however, heating to 150° causes the hydroxyketonic transformation of the chloroketone to proceed wholly with formation only of 3-hydroxy-2-butanone. In these conditions, on the other hand, 1-hydroxy-2-butanone does not isomerize to the secondary ketoalcohol. Consequently we can assume that the isomeric transformation is completed in the instant of action of the reagent on the chloroketone. Assuming that the chloroketone is enolized in the alkaline medium, the transformation may be represented as follows (via the allylic rearrangement):

$$CH_3-CH_2-CO-CH_2Cl \longrightarrow CH_3-CH=COH-CH_2Cl \longrightarrow CH_3-CHCl-COH=CH_2 \longrightarrow CH_3-CHOH-CO-CH_3.$$

(IX) (X)

Allylic rearrangement takes place in the enolic form of 1-chloro-2-butanol (IX) with formation of the enolic form of 3-chloro-2-butanone (X). Subsequently, due to hydrolysis, the chlorine is replaced by hydroxyl, and 3-hydroxy-2-butanone is formed.

It is evident that in the case of 1-hydroxy-2-butanone itself the allylic rearrangement with translocation of hydroxyl to the β-position does not take place since this ketoalcohol could not be isomerized to 3-hydroxy-2-butanone. It must be pointed out, however, that no proof has yet been forthcoming that the primary chloroketone can be isomerized to the secondary although this is extremely probable.

Polarographic Characterization of Chlorobutanones and Hydroxybutanones in 0.1 N NH_4Cl

Substance	Half-wave potential $E_{1/2}$ (in V)	Diffusion current constant $\frac{i_d}{c}$ (in $\frac{\mu A}{mole}$)	Consumption of electrons per mole of substance
1-Chloro-2-butanone	−1.065	3560	0.513
3-Chloro-2-butanone	−1.077	2248	0.353
1-Hydroxy-2-butanone	−1.790	1610	0.290
3-Hydroxy-2-butanone	−1.750	8960	0.470

Intramolecular oxidation-reduction transformations in chloroketones and ketoalcohols, when isomerization is accompanied by reduction of some carbon atoms and by oxidation of others, must be intimately bound up with the susceptibility to reduction of the isomerizing substances. For the comparison of ketoalcohols and chloroketones in respect of reduction we made use of the polarographic method. The results of the polarographic experiments were described in detail in an earlier paper by Bobrova and Tikhomirova-Sidorova [13] from which we quote some data in slightly modified and shortened form. We see from the table above that the primary chloroketone and 1-hydroxy-2-butanone, judging by all their electrochemical characteristics ($\frac{i_d}{c}$, α), are reduced with greater facility than the corresponding secondary compounds. This is in harmony with the fact that in the chloroketones $CH_3CH_2COCH_2Cl$ and $CH_3CHClCOCH_3$ the chlorine of the methyl group, due to its negative inductive effect, will more strongly repel the electrons of the carbonyl carbon than the atoms of chlorine of the ethyl group whose negative inductive effect overlaps with the positive inductive effect of the methyl group. Consequently, on the basis of these considerations, the primary chloroketone must be reduced more readily than the secondary isomer, as we found experimentally.

The polarographic behavior of the primary ketoalcohol is the opposite, in the given conditions, to that of the corresponding primary chloroketone in comparison with the secondary chloroketone.

In the light of the data obtained, the reduction of 3-hydroxy-2-butanone proceeds with greater facility than the reduction of 1-hydroxy-2-butanone; consequently greater difficulty must attend the intramolecular oxidation-reduction of the primary ketoalcohol, which is expected to result in reduction of the carbonyl group

and formation of the secondary ketoalcohol. The carbonyl group of the latter ketoalcohol possesses a greater susceptibility to reduction than that in the ketoalcohol with a primary alcohol group. According to the polarographic data, the transformation of 1-hydroxy-2-butanone into 3-hydroxy-2-butanone is hindered, in accord with our unsuccessful attempts to isomerize 1-hydroxy-2-butanone.

This again confirms that the transformation of α-hydroxybutyraldehyde into 3-hydroxy-2-butanone via 1-hydroxy-2-butanone is highly improbable.

The observation of the greater facility of reduction of 1-chloro-2-butanone in alkaline and neutral media is consistent with the intramolecular oxidation-reduction to acid in presence of metallic salts with or without addition of alkali. The susceptibility to reduction of 1-chloro-2-butanone, judging by all the polarographic data ($E_{1/2}$, $\frac{id}{c}$, α) exceeds that of 1-hydroxy-2-butanone, possibly due to the inductive effect of the chlorine atom.

No acidic transformation occurred in the case of the ketoalcohol with a primary alcohol group. On heating the chloroketone with 5% alkali solution and lead oxide, however, butyric acid was detected, although in low yield. The process may be represented by the equations:

$$CH_3-CH_2-CO-CH_2Cl \rightarrow CH_3CH_2\overset{\frown O \frown}{COH-CH_2} \rightarrow COOH-CH_2-CH_2-CH_3.$$

Publications by Favorsky [14] indicate that 3-chloro-2-butanone is converted into isobutyraldehyde in low yield.

Acidic products were not detected when 1-chloro-2-butanone was heated with sodium methoxide in anhydrous methyl alcohol.

According, however, to literature date [15], in the same conditions chloromethylbenzyl ketone $C_6H_5CH_2COCH_2Cl$ is completely converted into the ester of hydrocinnamic acid, while the primary chlorobenzylacetone $C_6H_5CH_2CH_2COCH_2Cl$ gives the corresponding acid in a yield of 8%. The aliphatic chloroketone $CH_3CH_2COCH_2Cl$ does not undergo the acidic transformation in presence of sodium ethoxide according to our experiments. We can, therefore, conclude that the phenyl radical favors the formation of acid from primary chloroketones.

It should be noted [16] that the acid transformation of chloroketones was developed in Favorsky's laboratory.

Previously proposed schemes of isomerization of α-hydroxyaldehydes via ketoalcohols with a primary alcohol group (the hypothesis of intermediate oxide-alcoholic forms [7] of Favorsky or that of intermediate dienols followed by allylic rearrangement [9] was used) must be modified in the light of the inability to obtain ketoalcohols with a primary alcoholic group on isomerization of α-hydroxyaldehydes; also they are not isomerized to alcohols with a secondary alcoholic group which are formed in experiments from α-hydroxyaldehydes.

Since the alcoholic-oxide scheme can be successfully applied to disubstituted glycolaldehydes, it is expedient to utilize for monosubstituted derivatives of glycolaldehyde, as was pointed out by E.D. Venus-Danilova and V.F. Kazimirova [9], a scheme according to which the α-hydroxyaldehyde changes into the dienol, which then undergoes the allylic rearrangement. Rejecting the primary ketoalcohol as an intermediate, we obtain such a scheme for the isomerization of monosubstituted glycolaldehydes:

$$R-CH_2-CHOH-CHO \rightarrow R-CH_2-COH=CHOH \rightarrow CH_2=COH-CHOH-R \rightarrow CH_3-CO-CHOH-R.$$

The transformation is effected in a weakly acid or weakly alkaline medium.

According to this scheme benzylglycolaldehyde must form phenylacetylcarbinol which is actually obtained by isomerization of the hydroxyaldehyde.

The proposed schemes, however, are only useful for a convenient representation of the transformations. Detailed kinetic studies are needed for clarification of the actual mechanism of the reactions in the conditions employed. Both in the cases considered and in other isomeric transformations we cannot exclude the probability (at least as a limiting case) of direct intramolecular rearrangement of the molecule under the influence of acid and alkali (hydrogen and hydroxyl ions) and heating [17].

EXPERIMENTAL

The primary and secondary chlorobutanones, hydroxybutanones and phenylacetol were synthesized for the experiments.

The chloroketones were prepared by chlorination of 2-butanone in a yield of 16% 1-chloro-2-butanone

(b.p. 137-138°, n_{α}^{20} 1.4311, d_4^{20} 1.0850) and 56% 3-chloro-2-butanone (b.p. 116-117°,). n_{α}^{20} 1.4210, d_4^{20} 1.0571). Properties and derivatives of the chlorobutanones have been described previously [12].

From the chloroketones were synthesized the corresponding ketoalcohols – 1-hydroxy-2-butanone from the primary and 3-hydroxy-2-butanone from the secondary chloroketone. The chloroketones were heated with absolutely dry potassium formate in a medium of anhydrous methanol; after fractionation in vacuum and in a stream of carbon dioxide, the ketoalcohol was obtained in a yield of 50%.

Preparation and Properties of 1-Hydroxy-2-butanone

We have already described this synthesis [12]. Here we give an example of a new modification of the synthesis.

A mixture of 60 g 1-chloro-2-butanone (b.p. 63° at 43 mm), 96 ml anhydrous methyl alcohol and 96 g dry potassium formate (m.p. 167°) was heated on a boiling water bath for 8 hours. The absolutely dry potassium formate was prepared by recrystallization from anhydrous ethyl alcohol and by prolonged drying in a vacuum pistolet over phosphorus pentoxide.

The reaction was carried out in a two-necked flask; in one neck was inserted a condenser closed with a calcium chloride tube; through the other neck was passed a stream of carbon dioxide. The end of the reaction was checked by a Beilstein test for halogen.

After termination of the heating, the liquid portion was filtered from the precipitate of potassium chloride which was washed with anhydrous ether. The ethereal extract was added to the main filtrate. After driving off the methyl formate (b.p. 32°) and ether on a water bath and then (in vacuum) the methanol (b.p. 20-25° at 20 mm), the following fractions were isolated:

First fraction b.p. 54–56° (18 mm), 1.8 g 2nd fraction b.p. 56–60° (18 mm), 25.7 g; resinous residue 6.4 g.

Redistillation of the 2nd fraction in a carbon dioxide stream gave 23.5 g ketoalcohol with b.p. 58° at 18 mm, equivalent to 49%.

1-Hydroxy-2-butanone is a transparent, colorless liquid with a characteristic pleasant odor; it readily reduces Fehling solution in the cold.

B.p. 54° at 18 mm, 57° at 22 mm, 78° at 60 mm, 86° at 72 mm, 153–154° at 765 mm; d_4^{20} 1.0186; n_{α}^{20} 1.4237; n_D^{20} 1.4248; MR_{α} 22.03; MR_D 22.09. $C_4H_8O_2$. calculated MR_{α} 22.09; MR_D 22.21.

0.1533 g sub: 0.3075 g CO_2; 0.1253 g H_2O. 0.1639 g sub: 0.3288 g CO_2; 0.1353 g H_2O. Found %: C 54.74, 54.74; H 9.01, 9.29. $C_4H_8O_2$. Calculated %: C 54.54; H 9.09;

The osazone (m.p. 115°) and the p-nitrophenylhydrazone (m.p. 228°) of propionylcarbinol have been described before [12].

1-Hydroxy-2-butanone semicarbazone was prepared by mixing equimolecular amounts of aqueous solutions of ketoalcohol, semicarbazide hydrochloride and potassium carbonate. On standing, the semicarbazone does not come down. The water is evaporated in vacuum and the dry residue is extracted with hot chloroform. The chloroform extract deposits a white crystalline precipitate which after recrystallization from water has m.p. 66°, identical with that of the semicarbazone of 1-hydroxy-2-butanone obtained in these conditions by Kling [18]. From 0.5 g ketoalcohol was obtained, after recrystallization, 0.36 g semicarbazone.

0.0964 g substance: 24.5 ml N_2 (18°, 764 mm). Found%: N 29.05. $C_5H_{11}O_2N_3$. Calculated %: N 28.96.

The 2,4-dinitrophenylhydrazone. The products of interaction of 1-hydroxy-2-butanone with 2,4-dinitrophenylhydrazine have not been described in the literature. By reacting equimolecular amounts of 1-hydroxy-2-butanone and 2,4-dinitrophenylhydrazine we obtained a yellow powder, which after two recrystallizations from alcohol had m.p. 141-142°, and corresponded in analysis with the 2,4-dinitrophenylhydrazone of the ketoalcohol.

0.0962 g substance: 17.5 ml N_2 (79°, 761 mm). 0.1004 g substance: 18.0 ml N_2 (19°, 761 mm). Found % N 21.10, 20.79. $C_{10}H_{12}O_5N_4$. Calculated %: N 20.87.

The 2,4-dinitrophenylosazone. On reacting 1-hydroxy-2-butanone with excess of 2,4-dinitrophenylhydrazine, an orange-red product is obtained which is insoluble in common organic solvents (alcohol, ethyl acetate, and pyridine). After digesting with alcohol and drying in a vacuum desiccator, a substance with m.p. 229-230° (0.70 g from 0.5 g ketoalcohol) is obtained; the analysis corresponds to the 2,4-dinitrophenylosazone of 1-hydroxy-2-butanone.

0.0937 g substance: 20.5 ml N_2 (19.5°, 760 mm). 4.190 mg substance: 0.9308 ml N_2 (18°, 735.6 mm). Found %: N 25.16, 25.24. $C_{16}H_{14}O_8N_8$. Calculated %: N 25.11.

Preparation and Properties of 3-hydroxy-2-butanone

3-Hydroxy-2-butanone was obtained by a slight modification of the above procedure for 1-hydroxy-2-butan-

one. 40 g 3-chloro-2-butanone, 64 g potassium formate, and 64 ml anhydrous methanol were placed in a glass tube, which was allowed to stand for 8 hours in an autoclave heated to 120°. After the usual working up and fractionation in a stream of carbon dioxide, 16.5 g of 3-hydroxy-2-butanone was obtained, equivalent to a yield of 51.0%.

3-Hydroxy-2-butanone is a colorless substance with a pleasant odor, which reduces Fehling solution in the cold.

B.p. 38° at 12 mm, 56° at 34 mm, 144° at 760 mm; n_D^{20} 1.4200; d_4^{20} 1.0101; MR_D 22.04. $C_4H_8O_2$. Calculated 22.21.

After a second distillation in vacuum, the pure substance starts to crystallize and in the course of a month it changes into a dense, white crystalline mass with m.p. 95° - the m.p. of the dimer of 3-hydroxy-2-butanone [19].

3-Hydroxy-2-butanone was converted by the usual method into the semicarbazone with m.p. 186-187° and the osazone with m.p. 243° in agreement with the melting points in the literature [20].

The p-nitrophenylhydrazone. Reaction of 3-hydroxy-2-butanone with an equimolecular amount of p-nitrophenylhydrazine gives a dark-red product which after recrystallization from a mixture of alcohol and pyridine has m.p. 246° and corresponds in analysis to 3-hydroxy-2-butanone p-nitrophenylhydrazone.

4.450 mg sub.: 0.7107 ml N_2 (20°, 754 mm). 2.855 mg sub.: 0.4510 ml N_2 (20°, 754 mm). Found %: N 18.46, 18.26. $C_{10}H_{13}O_3N_3$. Calculated %: N 18.83.

The 2,4-dinitrophenylhydrazone. Reaction of 2,4-dinitrophenylhydrazine with 0.5 g 3-hydroxy-2-butanone gave 1.27 g bright-orange powder which after recrystallization from a mixture of ethyl alcohol and ethyl acetate had m.p. 332° and corresponded in analysis to 3-hydroxy-2-butanone 2,4-dinitrophenylhydrazone, not described in the literature.

3.715 mg sub.: 0.670 ml N_2 (23°, 750 mm). 4.320 mg sub.: 0.789 ml N_2 (22°, 744 mm). Found %: N 20.60, 20.70. $C_{10}H_{12}O_5N_4$. Calculated %: N 20.87.

Experiments on Transformation of 1-Hydroxy-2-butanone

Experiments were run in the conditions selected by Danilov and Venus-Danilova [1] for transformation of α-hydroxyaldehydes; in no case, however, was the anticipated 3-hydroxy-2-butanone detected. For example, 1 g ketoalcohol was heated in an ampoule with 5 ml 1 % sulfuric acid on a glycerol bath at 140-145° for 5.5 hours. The sulfuric acid was then neutralized with potassium acetate. The contents of the ampoule were poured into a solution of 4 g phenylhydrazine in 50% acetic acid. The resultant osazone melted at 115° and did not give a depression with the osazone obtained from 1-hydroxy-2-butanone. In these conditions, therefore, the hydroxyketone transformation does not take place.

Heating with salts of zinc, copper and lead (in aqueous and alkaline media) also gave only derivatives of 1-hydroxy-2-butanone and ethylglyoxal (osazone m.p. 115°, disemicarbazone m.p. 228°) [12], and no derivatives 3-hydroxy-2-butanone and 2,3-butanedione were detected. Nor was butyric acid detected.

Transformation of 1-chloro-2-butanone

Some of the experiments were described in our previous paper [12]. It has already been pointed out that heating to 100-150° of the primary chloroketone in an alkaline medium with lead oxide and in an aqueous medium with silver carbonate gave derivatives of the secondary ketoalcohol. We now add the further information that heating of 1-chloro-2-butanone for 10 hours in an ampoule on a water bath at 100° with lead oxide in an aqueous medium (15 g chloroketone, 40 g PbO_2 and 150 ml water) yielded (after steam distillation) neutral products giving, in addition to 1-hydroxy-2-butanone osazone with m.p. 115°, an osazone with m.p. 243° and the 2,4-dinitrophenylhydrazone of 3-hydroxy-2-butanone with m.p. 332°; the two latter derivatives did not give depressions with specimens synthesized from authentic 3-hydroxy-2-butanone. The dimer of 3-hydroxy-2-butanone with m.p. 95° was isolated at the same time.

After distilling off the neutral product with water until the reaction with Fehling's solution was negative, the salts remaining in the flask were washed with solvents (ether, chloroform, alcohol, benzene and acetone) to remove resin, and the pure residue of salts was acidified with 2% sulfuric acid; distillation was then continued. A distillate was obtained with a weakly acidic reaction which did not give a double-bond reaction with bromine; it had a weak odor of butyric acid. In one experiment, for example, after heating 14 g chloroketone in an ampoule with 30 g lead oxide and 200 ml 5% KOH solution to 140° for 10 hours, 0.35 g butyric acid was found (by titration with 0.1 N sodium hydroxide solution) in 300 ml acid distillate.

0.1024 g of silver butyrate was obtained.

0.0472 g salt: 0.0260 g Ag. 0.0532 g salt 0.0295 g Ag. Found %: Ag 55.08, 55.45. $C_4H_7O_2Ag$. Calculated %: Ag 55.38.

Preparation, Properties and Transformations of Phenylglycidol

Convenient syntheses of phenylacetol have not been described in the literature. We proposed to obtain this ketoalcohol by isomerization of the oxide of cinnamyl alcohol —phenylglycidol.

Phenylglycidol was prepared by oxidation [21] of cinnamyl alcohol with benzoyl hydroperoxide in solution in chloroform or carbon tetrachloride.

We give one example of the synthesis: To a solution of 45 g hydroperoxide in 1700 ml CCl_4 in a 3-liter flask cooled with ice was added, with intensive stirring, a solution of 15 g cinnamyl alcohol in 750 ml CCl_4. The reaction proceeded for a period of 24 hours. Its progress was checked by the bromine test for the double bond. The solution was washed with potassium carbonate and the greater proportion of the CCl_4 was driven off in vacuum. The residue was dried with ignited sodium sulfate. The remainder of the solvent was distilled off in vacuum, at first on a water bath from a small flask, and then in a vacuum desiccator.

The substance was obtained in the form of a syrupy, readily crystallizing liquid with a pleasant odor. It is insoluble in water, soluble in alcohol, ether, carbon tetrachloride and chloroform; it does not react with bromine or Fehling solution (even hot). Iodine is liberated when the substance is heated with potassium iodide in acetic acid. Heating with iron chloride brings down ferric hydroxide which dissolves readily in dilute acids. The phenylglycidol resinifies badly when distilled.

B.p. 138° at 3 mm; n_D^{27} 1.5432; d_4^{27} 1.1512; MR_D 41.08. $C_9H_{10}O_2$. Calculated 41.26 (Hibbert [21] gives for phenylglycidol b.p. 135° at 4 mm and n_D^{27} 1.5427)

0.1012 g sub.: 0.2670 g CO_2; 0.0606 g H_2O. 0.0965 g sub.: 0.2530 g CO_2; 0.0595 g H_2O. Found %: C 71.93, 71.60; H 6.62, 6.85 $C_9H_{10}O_2$. Calculated %: C 72.00; H 6.66.

The phenylurethane of phenylglycidol was prepared in the usual manner: m.p. 89-90° (Hibbert [21] gives m.p. 87°).

0.0846 g sub.: 3.5 ml N_2 (19° at 765 mm). 0.0998 g sub.: 4.5 ml N_2 (19°, 765 mm). Found %: N 4.87, 5.22. $C_{16}H_{15}O_3N$. Calculated %: N 5.20.

The conditions of isomerization of phenylglycidol to the ketoalcohol, phenylacetol, were not established. However, after heating 5 g phenylglycidol with 100 ml 1% aqueous sulfuric acid in an ampoule at 140° for 5 hours, followed by reaction with semicarbazide, a semicarbazone with m.p. 132-133° was isolated; Darmon [22] reported the same m.p. for phenylacetol semicarbazone. Since the above conditions are the same as those in which the isomerization of phenylglycolaldehyde to phenylacetylcarbinol was realized, and since the semicarbazone of the latter with m.p. 194° [7] was not isolated in our case, we can assume that phenylacetol does not isomerize to phenylacetylcarbinol in the given conditions.

SUMMARY

1. A study was made of the isomeric transformations of α -hydroxyaldehydes with reference to the role of α -ketoalcohols in oxidation-reduction processes.

2. It was shown that the primary ketoalcohols, 1-hydroxy-2-butanone and phenylacetol, do not isomerize in the conditions of transformations of α -hydroxyaldehydes. For this reason we may infer that the isomerization of α -hydroxyaldehydes to secondary ketoalcohols does not proceed via the primary ketoalcohol.

3. Heating of the primary chloroketone, 1-chloro-2-butanone, to 100° with silver carbonate or lead hydroxide (in an aqueous or alkaline medium) converts it into 1-hydroxy-2-butanone and 3-hydroxy-2-butanone.

4. Heating of 1-chloro-2-butanone to 140° with lead hydroxide in an aqueous alkaline medium gives butyric acid in 3% yield.

5. The data from experiments on isomerization were confirmed by the polarographic method, which showed the primary ketoalcohol to be less susceptible than the secondary ketoalcohol to reduction and also revealed the facility of reduction of the primary chloroketone.

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α-HYDROXYISOBUTYRONITRILE AS A SOURCE OF HYDROCYANIC ACID IN ADDITION REACTIONS

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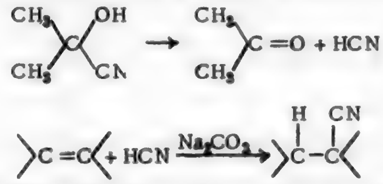
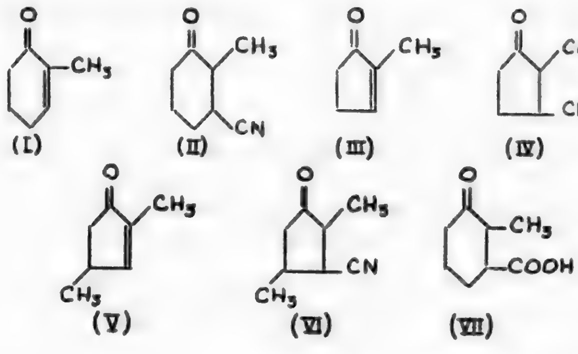
The addition of hydrocyanic acid to multiple bonds is effected, as we know, by means of liquid hydrocyanic acid or of cyanides of potassium and sodium, which, due to their high toxicity, are very inconvenient from the preparative standpoint. In this connection attention is deserving of the application of the simplest cyanohydrins in the synthesis of α-hydroxynitriles, starting from ketones [1, 2] and vinyl esters [3]. Although the addition of hydrocyanic acid to α,β-unsaturated olefinic compounds (ketones, aldehydes, nitriles, acids and their esters) has been exhaustively studied with reference to a great diversity of substances, there is no information at all in the literature regarding the possibility of utilization of the cyanohydrins of the simplest ketones in these reactions.

In the present investigation we showed that acetone cyanohydrin (α-hydroxyisobutyronitrile), in presence of an aqueous solution of sodium carbonate at 70-80° readily forms nitriles with various unsaturated compounds whose olefinic bond is activated by a carbonyl, nitrile or ester group. The reaction probably takes place in two stages: at first the α-hydroxyisobutyronitrile decomposes with release of free hydrocyanic acid, which then under the influence of sodium carbonate adds on to the active double bond:



In this manner 2-methyl-Δ^2-cyclohexene (I), 2-methyl-Δ^2-cyclopentenone (III) and 2,4-dimethyl-Δ^2-cyclopentenone (V) were converted into the ketonitriles (II), (IV) and (VI) in yields of 73, 77 and 55%, respectively.



The first two ketonitriles (II) and (IV) were isolated in the form of two stereoisomers, a liquid and a crystalline substance, which formed identical semicarbazones but different 2,4-dinitrophenylhydrazones. Since hydrolysis of the semicarbazones with hydrochloric acid gave the crystalline isomers, the latter in all probability possess the more stable trans-configuration. It is interesting to note that 2,4-dimethyl-Δ^2-cyclopentenone (V) forms only one isomer of 2,4-dimethyl-3-cyanocyclopentanone (VI). For confirmation of the structure of the obtained substances, both isomers of 2-methyl-3-cyanocyclohexanone (II) were converted by boiling with dilute caustic alkali into the known 2-methyl-3-ketocyclohexane carboxylic acid (VII). Reaction of acrylonitrile with α-hydroxyisobutyronitrile gives succinonitrile (VIII) in 88% yield, whereas with hydrocyanic acid [4] and potassium cyanide [5] the yields do not exceed 84%. Methyl acrylate proved to be considerably less reactive; with α-hydroxyisobutyronitrile it gives methyl β-cyanopropionate (IX) in a yield of only 50% after many hours' heating in a closed vessel.

$NCCH_2CH_2CN$ (VIII) $NCCH_2CH_2COOCH_3$. (IX)

We thus established that α-hydroxyisobutyronitrile can be used as a source of hydrocyanic acid not only for the synthesis of α-hydroxynitriles when starting from ketones, but also in other addition reactions.

The simplicity and convenience of the method and the mild reaction conditions make the cyanohydrin method of preparation of nitriles extremely valuable from the preparative standpoint.

EXPERIMENTAL

2-Methyl-3-Cyanocyclohexanone (II)

A mixture of 3 g 2-methyl-Δ^2-cyclohexenone (I) (b.p. 55-56° at 9 mm, n_D^{20} 1.4865) [6], 3 g α-hydroxyisobutyronitrile, 8 ml methanol and 0.2 g sodium carbonate in 3 ml water is heated under a reflux condenser on a water bath at 70-80° for 3 hours. After cooling, the reaction mixture is extracted with ether, the solvent is driven off, and the residue distilled in vacuum. Yield 2.7 g (73%) of a mixture of the isomers of 2-methyl-3-cyanocyclohexanone (II) with b.p. 134-138° at 10 mm.

Freezing and distillation of this mixture gave 0.5 g of the crystalline isomer (II) with m.p. 57-58 (from a mixture of benzene and ligroin).

Found %: C 69.80, 69.95; H 8.19, 8.22; N 10.20, 10.22. $C_8H_{11}ON$. Calculated %: C 70.1; H 8.0; N 10.2.

The semicarbazone melts at 223-225° with decomposition (from aqueous methanol).

Found %: N 28.65, 28.73. $C_9H_{14}ON_4$. Calculated %: N 28.7.
Hydrolysis of this semicarbazone with HCl gives the original cyanoketone (II) with m.p. 57-58°.
The 2,4-dinitrophenylhydrazone of the crystalline cyanoketone (II) melts at 208-209° (from aqueous methanol).

Found %: N 22.40, 22.55, $C_{14}H_{15}O_4N_5$. Calculated %: N 22.1.

The liquid isomer of the cyanoketone (II) has b.p. 136-138° at 10 mm; n_D^{20} 1.4725.

Found %: C 70.05, 69.94; H 8.18, 8.01; N 10.05, 9.98. $C_8H_{11}ON$. Calculated %: C 70.1; H 8.0; N 10.2.

Its 2,4-dinitrophenylhydrazone melts at 191-192° (from aqueous methanol) and gives a considerable depression with the 2,4-dinitrophenylhydrazone of the crystalline isomer.

Found %: N 22.19, 21.87. $C_{14}H_{15}O_4N_5$. Calculated %: N 22.1.

The liquid cyanoketone (II) forms the above-described semicarbazone of the crystalline isomer with m.p. 223-225°.

2-Methyl-3-cyanocyclopentanone (IV)

A mixture of 10 g 2-methyl-Δ^2-cyclopentenone (II) (b.p. 52-53° at 15 mm, n_D^{20} 1.4770) [6], 10 g α-hydroxyisobutyronitrile, 15 ml methanol and 0.5 g sodium carbonate in 10 ml water was refluxed for 3 hours. After working-up as above, 10 g (77%) of a mixture of the isomers of 2-methyl-3-cyanocyclopentanone (IV) with b.p. 88-89° at 2 mm was obtained. Freezing and distillation of this mixture gave 3 g of the crystalline isomer with m.p. 49-50° (from a mixture of benzene and ligroin).

Found %: C 67.79, 67.98; H 7.45, 7.53; N 11.30, 11.35. C_7H_9ON. Calculated %: C 68.2; H 7.3; N 11.3.

The semicarbazone melts at 226-227° with decomposition (from methanol).

Found %: 31.35, 31.48. $C_8H_{12}ON_4$. Calculated %: N 31.4.

Treatment with hydrochloric acid converts this semicarbazone into the original crystalline cyanoketone (IV) with m.p. 49-50°.

The 2,4-dinitrophenylhydrazone of the crystalline cyanoketone (IV) melts at 192-193° (from aqueous methanol).

Found %: N 23.15, 23.27. $C_{13}H_{13}O_4N_5$. Calculated %: N 23.1.

The liquid isomer of the cyanoketone (IV) has b.p. 88-89° at 2 mm; n_D^{22} 1.4617.

Found %: C 68.11, 68.38; H 7.53; 7.43; N 11.40, 11.60. C_7H_9ON. Calculated %: C 68.2; H 7.3; N 11.3.

Its 2,4-dinitrophenylhydrazone melts at 200-201° (from aqueous methanol) and gives a considerable depression with the 2,4-dinitrophenylhydrazone of the crystalline isomer.

Found %: N 23.25, 23.37. $C_{13}H_{13}O_4N_5$. Calculated %: N 23.1.

The liquid cyanoketone (IV) forms the above-described semicarbazone of the crystalline isomer with m.p. 226-227°.

2,4-Dimethyl-3-cyanocyclopentanone (VI)

The reaction is carried out as described above.

From 8 g 2,4-dimethyl-Δ^2-cyclopentenone (V) (b.p. 50-52° at 9 mm, n_D^{22} 1.4670) [6] was obtained 5 g (55%) 2,4-dimethyl-3-cyanocyclopentanone (VI) with b.p. 119-121° at 11 mm; n_D^{20} 1.4580.

Found %: C 69.97, 69.94; H 8.17, 8.21; N 10.08, 10.03. $C_8H_{11}ON$. Calculated %: C 70.1; H 8.0; N 10.2.

The semicarbazone melts at 204-206° with decomposition (from aqueous methanol).

Found %: N 28.55, 28.54. $C_9H_{14}ON_4$. Calculated %: N 28.7.

The 2,4-dinitrophenylhydrazone melts at 188-189° (from aqueous methanol).

Found %: N 22.38, 22.45. $C_{14}H_{15}O_4N_5$. Calculated %: N 22.1.

Hydrolysis of 2-methyl-3-cyanocyclohexanone

0.5 g of a mixture of the isomers of 2-methyl-3-cyanocyclohexanone (II) is boiled with a solution of 1.5 g KOH in 5 ml water for 7 hours. The cooled solution is acidified with dilute (1:1) hydrochloric acid until acid to congo and then extracted with chloroform. After driving off the solvent, the residue crystallizes almost completely. Yield 0.4 g (70%) 2-methyl-3-ketocyclohexane carboxylic acid (VII) with m.p. 96-97° (from n-hexane); the semicarbazone melts at 205-206° with decomposition (from aqueous methanol). The literature [7] reports m.p. 97° for this acid and m.p. 205° with decomposition for its semicarbazone.

Succinonitrile

A mixture of 5.3 g acrylonitrile, 9 g α-hydroxyisobutyronitrile and 0.5 g sodium carbonate in 3 ml water is refluxed at 70-75° for 3 hours. After cooling, the reaction product is extracted with chloroform and distilled in vacuum. Yield 7 g (88%) of succinonitrile (VIII) with b.p. 149-150° at 16 mm and m.p. 53-54° [5].

Methyl β-cyanopropionate

A mixture of 8.6 methyl acrylate, 9 g α-hydroxyisobutyronitrile and 0.5 g sodium carbonate in 8 ml water is heated in a sealed vessel at 70-80° for 15 hours. After cooling, the reaction product is extracted with ether and distilled at atmospheric pressure. Yield 5.6 g (50%) methyl β-cyanopropionate (IX) with b.p. 210-212°; n_D^{20} 1.4250.

The literature gives b.p. 215°; n_D^{20} 1.4243 [8].

SUMMARY

It is found that α-hydroxyisobutyronitrile can serve as a source of hydrocyanic acid in addition reactions at double bonds activated by carbonyl, nitrile and ester groups.

This method was used, starting from 2-methyl-Δ^2-cyclohexenone (I), 2-methyl-Δ^2-cyclopentenone (III), 2,4-dimethyl-Δ^2-cyclopentenone (V), acrylonitrile and methyl acrylate, to give respectively the nitriles (II), (IV), (VI), (VIII) and (IX) in yields of 73, 77, 55, 88, and 50% of the theoretical.

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CYANOETHYLATION OF CYCLIC β-DIKETONES

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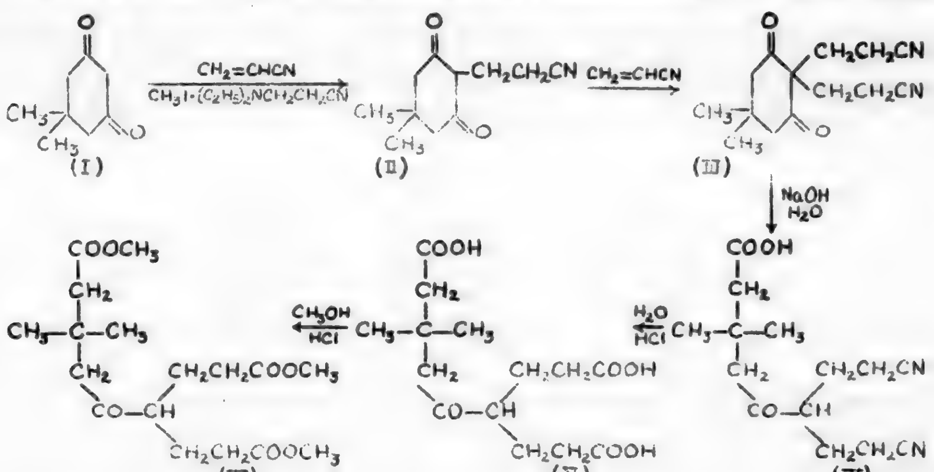
Following our discovery that cyclic β-diketones enter into addition reactions with various vinylketones [1], it seemed of interest to investigate the reaction of cyclic β-diketones with other unsaturated compounds, in particular acrylonitrile. The introduction of the cyanoethyl group into the dihydroresorcinol (XIII) molecule and its derivatives should permit access to various difficultlyaccessible organic compounds of the aliphatic, cyclic and heterocyclic series.

A number of American [2 3] and English investigators [4] have attempted to effect the cyanoethylation of dihydroresorcinol (XIII), 5,5-dimethyl-1,3-cyclohexanedione (i.e. dimedon) (I) and similar compounds but were unsuccessful. These authors reached the conclusion that cyclic β-diketones in general cannot enter into addition reactions with acrylonitrile. This assertion has proved erroneous since we have shown that 5,5-dimethyl-1,3-cyclohexanedione (I), methyldihydroresorcinol (VIII) and dihydroresorcinol (XIII) in presence of aqueous NaOH at 100° readily and completely react with acrylonitrile to form various addition products, depending on the structure of the β-diketone, the amount of alkali and the reactants used.

Reaction of 5,5-dimethyl-1,3-cyclohexanedione (I) with excess of acrylonitrile in presence of one equivalent of alkali leads to formation of mono- and bis-adducts (II) and (III) together with a considerable amount of the dicyanoketoacid (IV) formed from the bis-adduct (III) by hydrolytic cleavage of the dihydroresorcinol ring. Hydrolysis of the dicyanoketo acid (IV) gives 2,2-dimethyl-4-keto-5-(2'-carboxethyl)-heptane-1,7-dicarboxylic acid (V) which with a methanol solution of hydrogen chloride forms the trimethyl ester (VI). The structure of the prepared compounds was confirmed by special experiments which showed that in the above-specified conditions (β-cyanoethyl)-5,5-dimethyl-1,3-cyclohexanedione (II) is transformed into the bis-adduct (III) and the latter into the keto acid (IV).

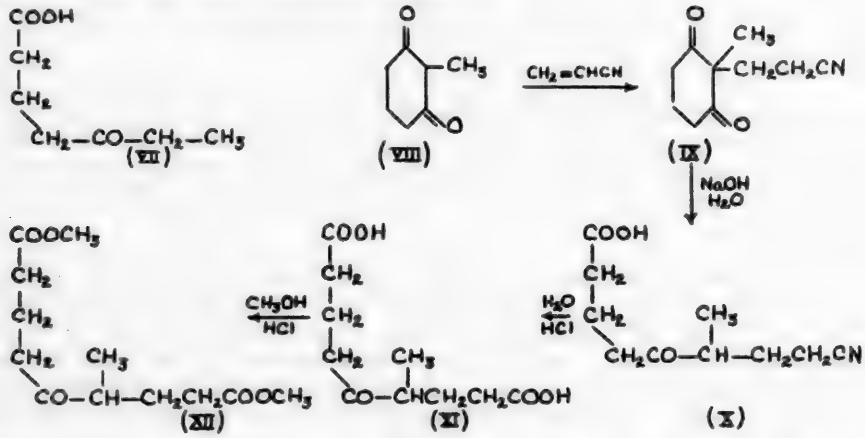
When using 1/6 equivalent of alkali and excess of acrylonitrile, the cyanoethylation of 5,5-dimethyl-1,3-cyclohexanedione (I) gives mainly the bis-adduct (III). The melting point of (β-cyanoethyl)-5,5-dimethyl-1,3-cyclohexanedione (II) exactly coincides with that of the substance obtained by English investigators [4] from the sodium derivative of 5,5-dimethyl-1,3-cyclohexanedione and β-diethylaminopropionitrile methiodide.



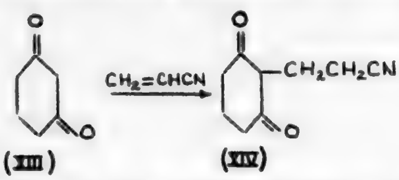
Heating of methyldihydroresorcinol (VIII) with acrylonitrile in an aqueous dioxane medium in presence of an equivalent of caustic alkali leads exclusively to the cyanoketo acid (X) which is formed by hydrolytic cleavage of (β-cyanoethyl)-methyldihydroresorcinol (IX). The suggestion that hydrolytic cleavage of methyldihydroresorcinol (VIII) itself to γ-propionylbutyric acid (VII) takes place during the reaction, followed by cyanoethylation of the latter, was not confirmed, since the authentic keto acid (VII) in the same conditions does not react with acrylonitrile.

On hydrolysis, the cyanoketo acid (X) is transformed into 4-keto-5-methylheptane-1,7-dicarboxylic acid (XI) which forms the dimethyl ester (XII) under the action of methanol in presence of hydrogen chloride.

In presence of 1/6 equivalent of NaOH the cyanoethylation of methyldihydroresorcinol leads in good yield to the normal product of addition (IX) which actually proved very sensitive to the action of alkali and readily underwent cleavage to form the above-mentioned keto acid (X).



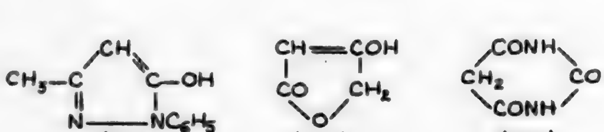
The cyanoethylation of dihydroresorcinol (XIII) is a more complex process. Individual products of the reaction could not be isolated when using 1/6 equivalent of alkali, but a mixture of compounds from which (β-cyanoethyl)-dihydroresorcinol (XIV) was isolated was formed when using an equivalent of alkali.



(XIII) (XIV)

The cyanoethylation of cyclic β-diketones also proceeds at temperatures below 100°. In these conditions, however, the reaction velocity is considerably reduced. Thus, for example, 5,5-dimethyl-1,3-cyclohexanedione when heated with excess of acrylonitrile at 60-70° in an aqueous dioxane medium in presence of 1/6 equivalent of alkali gave only the monocyanoethyl derivative in a yield of 56%.

In the light of the results obtained, doubt must be cast upon the correctness of the English investigators' [4] hypothesis of the mechanism of the reaction of the sodium derivative of 5,5-dimethyl-1,3-cyclohexanedione with β-diethylaminopropionitrile methiodide, which involved the intermediate formation of acrylonitrile. Our own method may be suitable also for the cyanoethylation of phenylmethylpyrazolone (XV), tetronic acid (XVI), barbituric acid (XVII) and similar substances of an acidic character.



(XV) (XVI) (XVII)

EXPERIMENTAL

5,5-Dimethyl-1,3-cyclohexanedione (I) (m.p. 144-145°) was obtained by the action of malonic ester on mesityl oxide followed by hydrolysis of the reaction product [5].

Methyldihydroresorcinol (VIII) (m.p. 208-209°) was obtained by methylation of dihydroresorcinol [1].

Dihydroresorcinol (XIII) (m.p. 104-105°) was prepared by hydrogenation of resorcinol [6].

Cyanoethylation of 5,5-dimethyl-1,3-cyclohexanedione

1. To a solution of the Na-derivative of 5,5-dimethyl-1,3-cyclohexanedione (I), prepared from 0.8 g NaOH, 5 ml water and 2.8 g 5,5-dimethyl-1,3-cyclohexanedione, was added 4 g acrylonitrile in 8 ml dioxane. The mixture was refluxed for 1.5 hours.

Evaporation of the solution in vacuum gave 1.1 g di-(β-dicyanoethyl)-5,5-dimethyl-1,3-cyclohexanedione (III) with m.p. 146-147° (from aqueous methanol).

Found %: C 68.55, 68.40; H 7.50, 7.30; N 11.43, 11.53. $C_{14}H_{18}O_2N_2$. Calculated %: C 68.2; H 7.3; N 11.4.

Acidification of the alkaline mother liquor with conc. hydrochloric acid followed by extraction with chloroform gave 3.8 g viscous oil which partially crystallized after addition of ether. Yield 0.5 g (β-cyanoethyl)-5,5-dimethyl-1,3-cyclohexanedione (II) with m.p. 151-152° (from water).

Found %: C 68.46, 68.55; H 8.11, 8.04; N 7.19, 7.30. $C_{11}H_{15}O_2N$. Calculated %: C 68.4; H 7.8; N 7.3.

On standing, the mother liquor crystallized almost completely to give 1.5 g dicyanoketo acid (IV) with m.p. 62-63° (from a mixture of ether and n-hexane).

Found%: C 63.61, 63.72; H 8.04, 7.86; N 10.30, 10.24. $C_{14}H_{20}O_3N_2$. Calculated %: C 63.6; H 7.6; N 10.6.
Found: equiv (titration) 260, 262. $C_{14}H_{20}O_3N_2$. Calculated: equiv. 264.

2. To a solution of 0.07 g NaOH in 5 ml of water was added 1.4 g 5,5-dimethyl-1,3-cyclohexane dione (I) and then 3 g acrylonitrile in 5 ml dioxane. The mixture was refluxed for 3.5 hours. Evaporation of the solution brought down 2 g (81%) crystals with m.p. 146-147° (from aqueous methanol), which did not give a depression with the above-described bis-adduct (III).

3. To a solution of 0.025 g NaOH in 3 ml water was added 0.5 g 5,5-dimethyl-1,3-cyclohexane dione and 2 g acrylonitrile in 3 ml dioxane. The mixture was heated at 60-70° for 5 hours. On evaporation of the solution in vacuum 0.4 g (56%) of the mono-adduct (II) came down; m.p. 150-152° (from water).

Hydrolytic Cleavage of Di-(β-cyanoethyl)-5,5-dimethyl-1,3-cyclohexanedione.

A mixture of 0.5 g of (III), m.p. 146-147°, and 1 g potassium carbonate in 10 ml water was refluxed for 15 minutes. Acidification of the solution with conc. HCl and extraction with chloroform gave 0.4 g (74%) dicyanoketo acid (IV), m.p. 62-63° (from a mixture of ether and n-hexane). Hydrolytic cleavage of (III) also occurs in alkali.

Transformation of (II) into the bis-Adduct (III)

To a solution of 0.023 g NaOH in 8 ml water were added 0.5 g (β-cyanoethyl)-5,5-dimethyl-1,3-cyclohexanedione (II) with m.p. 151-152° and 2 g acrylonitrile in 5 ml dioxane. The mixture was refluxed for 2 hours. On evaporation of the solution in vacuum, 0.4 g (59%) crystals with m.p. 146-147° (from aqueous methanol) came down; they did not give a depression with the dicyanoethyl derivative (III).

Trimethyl 2,2-dimethyl-4-keto-5-(2'-carboxethyl)-heptane-1,7-dicarboxylate

2.6 g dicyanoketo acid (IV) with m.p. 62-63° and 30 ml dilute (1:1) hydrochloric acid were refluxed for 6 hours. The solution was evaporated to dryness in vacuum; the residual crude tricarboxylic acid (V) was dissolved in acetone to free it from ammonium chloride; after driving off the solvent, it was mixed with 50 ml saturated solution of hydrochloric acid in methanol.

After standing for 24 hours at room temperature, the solution was evaporated in vacuum; the residue was treated with sodium carbonate solution and the reaction product was extracted with ether and fractionated in vacuum. Yield 2.4 g trimethyl 2,2-dimethyl-4-keto-5-(2'-carboxethyl)-heptane-1,7-dicarboxylate (VI) with b.p. 187-189° at 1 mm; n_D^{22} 1.4584.

Found %: C 59.02, 59.02; H 8.20, 8.30. $C_{17}H_{28}O_7$. Calculated %: C 59.2; H 8.1.

The compound does not form a crystalline semicarbazone or 2,4-dinitrophenylhydrazone.

2,2-Dimethyl-4-keto-5-(2'-carboxethyl)-heptane-1,7-dicarboxylic acid

1 g trimethyl ester (VI) and 10 ml dilute (1:1) hydrochloric acid were refluxed for 6 hours. After the volatile products had been distilled off in vacuum, the residue crystallized. Yield 0.6 g 2,2-dimethyl-4-keto-5-(2'-carboxethyl)-heptane-1,7-dicarboxylic acid (V), m.p. 109-110° (from a mixture of benzene and dioxane).

Found %: C 55.53, 55.71; H 7.12, 7.23. $C_{14}H_{22}O_7$. Calculated %: C 55.6; H 7.3. Found: equiv. (titration) 96.98. $C_{14}H_{22}O_7$. Calculated: equiv. 100.7.

Cyanoethylation of methyldihydroresorcinol

1. To a solution of the sodium derivative of methyldihydroresorcinol (VIII) prepared from 0.9 g NaOH, 5 ml water and 3 g diketone was added 4 g acrylonitrile in 8 ml dioxane. The mixture was refluxed for 3 hours. Acidification and extraction of the solution with chloroform gave 3.5 g (74%) of the cyanoketo acid (X) with b.p. 200-203° at 2 mm; n_D^{20} 1.4763.

Found %: C 61.12, 61.12, H 8.06, 7.95; N 7.50, 7.65. $C_{10}H_{15}O_3N$. Calculated %: C 60.9; H 7.7; N 7.2.
Found: equiv. (titration) 194, 196. $C_{10}H_{15}O_3N$. Calculated: equiv. 197.

The substance does not form a crystalline semicarbazone or 2,4-dinitrophenylhydrazone.

2. To a solution of 0.1 g NaOH in 8 ml water were added 2 g methyldihydroresorcinol (VIII) and 4 g acrylonitrile in 5 ml dioxane. The mixture was refluxed for 3 hours and then extracted with ether. After the solvent had been driven off, the residue was distilled in vacuum to give 2.3 g (82%) (β-cyanoethyl)-methyldihydroresorcinol (IX) with b.p. 142-144° at 1 mm; n_D^{20} 1.4890.

Found %: C 67.13, 67.05; H 7.21, 7.24; N 8.16, 8.22. $C_{10}H_{13}O_2N$. Calculated %: C 67.0; H 7.3; N 7.8.

Hydrolytic cleavage of (β-cyanoethyl)-methyldihydroresorcinol

A mixture of 3 g (β-cyanoethyl)-methyldihydroresorcinol (IX) and 1 g NaOH in 20 ml water was refluxed for one-half hour. Acidification followed by extraction with chloroform gave 2.5 g cyanoketo acid (X) with b.p. 200-202° at 2 mm; n_D^{20} 1.4760.

Dimethyl 4-keto-5-methylheptane-1,7-dicarboxylate

2 g cyanoketo acid (X) in 30 ml dilute (1:1) hydrochloric acid was refluxed for 6 hours. The solution was evaporated to dryness in vacuum; the residual dicarboxylic acid (XI) was freed from ammonium chloride as described above and mixed with a saturated methanol solution of hydrochloric acid (20 ml). After standing for 24 hours at room temperature, the solution was evaporated to dryness; the residue was treated with sodium carbonate solution and the reaction product was extracted with ether and distilled to give 1.8 g dimethyl 4-keto-5-methylheptane-1,7-dicarboxylate (XII) with b.p. 142-144° at 2 mm, n_D^{23} 1.4473.

Found %: C 58.77, 58.72; H 7.97, 8.11, $C_{12}H_{20}O_5$. Calculated %: C 59.0; H 8.2

The compound does not give a crystalline semicarbazone or 2,4-dinitrophenylhydrazone.

Hydrolysis with dilute hydrochloric acid of the dimethyl ester (XII) gave the oily dicarboxylic acid (XI) which failed to crystallize.

Cyanoethylation of dihydroresorcinol

1. To a solution of the Na derivative of dihydroresorcinol (XIII), prepared from 1.2 g NaOH, 8 ml water and 3.5 g diketone was added 5 g acrylonitrile in 10 ml dioxane. After refluxing for 2.5 hours, the solution was acidified with conc. hydrochloric acid and extracted with chloroform to give 1.2 g (23%) (β-cyanoethyl)-dihydroresorcinol (XIV) with m.p. 203-204° (from water).

Found %: C 65.17, 65.10; H 6.77, 6.68; N 8.91, 8.90. $C_9H_{11}O_2N$. Calculated %: C 65.4; H 6.77; N 8.5.

2. To a solution of 0.05 g NaOH in 5 ml water were added 1.4 g dihydroresorcinol (XIII) and 4 g acrylonitrile in 3 ml dioxane. The mixture was refluxed for 6 hours. On cooling, 2 g white powder came down; it decomposed at 190-200° and was insoluble in water and organic solvents.

SUMMARY

1. The incorrectness was shown of the claims of some American and English investigators that cyclic β-diketones are not amenable to cyanoethylation.

2. A method was discovered for cyanoethylation of cyclic β-diketones consisting in heating with acrylonitrile at 100° in an aqueous dioxane medium in presence of caustic alkali.

3. Reaction of 5,5-dimethyl-1,3-cyclohexanedione (I) with acrylonitrile leads to good yields of (β-cyanoethyl)-5,5-dimethyl-1,3-cyclohexanedione (II), di-(β-cyanoethyl)-5,5-dimethyl-1,3-cyclohexanedione (III) and a dicyanoketo acid (IV).

4. Cyanomethylation of methyldihydroresorcinol (VIII) gives (β-cyanoethyl)-methyldihydroresorcinol (IX) and a cyanoketo acid (X) in a yield of about 80%.

5. Cyanoethylation of dihydroresorcinol (XIII) gave (β-cyanoethyl)-dihydroresorcinol (XIV) in a yield of 23%.

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ESTERS OF ARYLSULFONIMIDOPHOSPHORIC ACIDS

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In recent years [1] trichlorophosphazosulfonaryls have become easily accessible substances. They are exceptionally reactive and can serve as starting materials for the preparation of a large number of compounds of the most diverse types.

In previous papers [2] results were reported of a study of the hydrolysis and acidolysis of trichlorophosphazosulfonaryls, and the products of reaction of trichlorophosphazosulfonaryls with ammonia and aromatic amines were described.

In the present paper are communicated the results of a study of reactions of trichlorophosphazosulfonaryls with sodium alkoxides, and the resultant aliphatic esters of arylsulfonimidophosphoric acids are described. In addition, the synthesis and properties of α- and β-trichlorophosphazosulfonnaphthyls are described.

On slowly running a benzene solution of trichlorophosphazosulfonaryl into a solution of sodium alkoxide in the corresponding alcohol with thorough stirring and cooling with iced water, the full esters of the arylsulfonimidophosphoric acids can be obtained in a yield of 70-80%. The trialkyl esters of the arylsulfonimidophosphoric acids are formed according to the scheme:

$$ArSO_2N{=}PCl_3 + 3AlkONa \rightarrow ArSO_2N{=}P(OAlk)_3 + 3NaCl.$$

Always accompanying the full esters as secondary products are the dialkyl esters of arylsulfonamidophosphoric acids. Formation of the latter is explained either by interaction of the full esters with still unreacted sodium alkoxide

$$ArSO_2N{=}P(OAlk)_3 + AlkONa \longrightarrow ArSO_2NNaPO(OAlk)_2 + AlkOAlk,$$

or (less probably) by direct reaction according to the scheme:

$$ArSO_2N{=}PCl_3 + 3AlkONa \longrightarrow ArSO_2NNa{-}PO(OAlk)_2 + AlkCl + 2NaCl.$$

The yield of dialkyl esters is 10-20%. The total yield of trialkyl and dialkyl esters is 90-95%.

Reaction of trichlorophosphazosulfonaryls with sodium alkoxides gives, in addition to trialkyl and dialkyl esters, small quantities of by-products of unknown structure which impart to the reaction mixture and to the crude, unpurified products an extraordinarily unpleasant odor.

Reaction of trichlorophosphazosulfonaryls with sodium alkoxides gave the trimethyl, triethyl and tri-n-butyl esters of phenyl-, o- and p-tolyl, and α- and β-naphthylsulfonimidophosphoric acids. Secondary products were the corresponding dialkyl esters.

The tri- and dialkyl esters obtained are set forth in Table 1.

The trialkyl esters are colorless crystalline substances or viscous, oily liquids; they are tasteless and odorless. The triethyl and trimethyl esters are very readily soluble in acetone, benzene, and chloroform, readily soluble in ether, hot alcohol and hot carbon tetrachloride. The tri-n-butyl esters are miscible in all proportions with the above solvents. The trialkyl esters are insoluble in water.

The trimethyl and the solid triethyl esters readily crystallize from ether, carbon tetrachloride and alcohol.

Distillation at atmospheric pressure decomposes the trialkyl esters, but they distil without decomposition in vacuum.

Chemically the full esters of arylsulfonimidophosphoric acids are stable and neutral substances. They are perfectly stable to water and do not react with it even after prolonged heating. They are also stable toward dilute mineral acids at room temperature but at the boil they are hydrolyzed, although very slowly. Thus, heating at the boil for an hour of 0.001 mole full ester with 25 ml 0.2 N aqueous hydrochloric acid caused no change in the ester and it could be recovered to the extent of 95%. The stability of the full esters of arylsulfonimidophosphoric acids toward weak aqueous solutions of mineral acids is evidently explicable by their insolubility in water. Actually, if in place of an aqueous solution, we take a 0.2 N aqueous alcoholic solution of hydrochloric acid (5 ml 1 N aqueous solution of acid + 20 ml alcohol), in which the full esters are readily soluble, then on

TABLE 1

Trialkyl Esters of Arylsulfonimidophosphoric Acids and Dialkyl Esters of Arylsulfonamidophosphoric Acids

Formula of prepared ester	Yield (in %)	Melting point
$C_6H_5SO_2N{=}P(OCH_3)_3$	75.9	38-40°
$C_6H_5SO_2NHPO(OCH_3)_2$	15.1	108-109
o-$CH_3C_6H_4SO_2N{=}P(OCH_3)_3$	76.0	74-75
o-$CH_3C_6H_4SO_2NHPO(OCH_3)_2$	20.4	145-146
p-$CH_3C_6H_4SO_2N{=}P(OCH_3)_3$	80.5	44-45
p-$CH_3C_6H_4SO_2NHPO(OCH_3)_2$	8.9	110-111
α-$C_{10}H_7SO_2N{=}P(OCH_3)_3$	71.7	84-85
α-$C_{10}H_7SO_2NHPO(OCH_3)_2$	25.1	164-165
β-$C_{10}H_7SO_2N{=}P(OCH_3)_3$	79.6	93-94
β-$C_{10}H_7SO_2NHPO(OCH_3)_2$	12.7	144-145
$C_6H_5SO_2N{=}P(OC_2H_5)_3$	81.5	Liquid
$C_6H_5SO_2NHPO(OC_2H_5)_2$	6.8	111-112
o-$CH_3C_6H_4SO_2N{=}P(OC_2H_5)_3$	82.1	35-37
o-$CH_3C_6H_4SO_2NHPO(OC_2H_5)_2$	9.7	97-98
p-$CH_3C_6H_4SO_2N{=}P(OC_2H_5)_3$	78.7	Liquid
p-$CH_3C_6H_4SO_2NHPO(OC_2H_5)_2$	7.8	105-106
α-$C_{10}H_7SO_2N{=}P(OC_2H_5)_3$	86.4	94-95
α-$C_{10}H_7SO_2NHPO(OC_2H_5)_2$	8.16	154-155
β-$C_{10}H_7SO_2N{=}P(OC_2H_5)_3$	75.4	51-52
β-$C_{10}H_7SO_2NHPO(OC_2H_5)_2$	20.4	161-162
$C_6H_5SO_2N{=}P(OC_4H_9\text{-n.})_3$	85.1	Liquid
o-$CH_3C_6H_4SO_2N{=}P(OC_4H_9\text{-n.})_3$	88.7	Liquid
α-$C_{10}H_7SO_2N{=}P(OC_4H_9\text{-n.})_3$	86.9	Liquid
β-$C_{10}H_7SO_2N{=}P(OC_4H_9\text{-n.})_3$	90.9	Liquid

TABLE 2

Hydrolysis of 0.001 mole of full Esters of Arylsulfonimidophosphoric acids with 0.2 N Aqueous Alcoholic Hydrochloric Acid

In the course of an hour

Formula of ester subjected to hydrolysis	Amount of unreacted ester		Yield of dialkyl ester	
	(in g)	(in %)	(in g)	(in %)
$C_6H_5SO_2N{=}P(OCH_3)_3$	0	0	0.19	71.7
o-$CH_3C_6H_4SO_2N{=}P(OCH_3)_3$	0	0	0.20	71.6
α-$C_{10}H_7SO_2N{=}P(OCH_3)_3$	0	0	0.30	95.1
β-$C_{10}H_7SO_2N{=}P(OCH_3)_3$	0	0	0.29	92.0
$C_6H_5SO_2N{=}P(OC_2H_5)_3$	0.14	43.6	0.15	51.1
o-$CH_3C_6H_4SO_2N{=}P(OC_2H_5)_3$	0.18	53.7	0.11	35.8
α-$C_{10}H_7SO_2N{=}P(OC_2H_5)_3$	0.23	61.9	0.10	29.1
β-$C_{10}H_7SO_2N{=}P(OC_2H_5)_3$	0.17	45.8	0.17	49.5
α-$C_{10}H_7SO_2N{=}P(OC_4H_9)_3$	0.30	66.7	Not determined	

heating to the boil for an hour the full methyl esters are completely hydrolyzed; the ethyl and butyl esters are less easily hydrolyzed. Thus the tri-n-butyl ester of α-naphthylsulfonimidophosphoric acid is only hydrolyzed to the extent of 33.3% when boiled for an hour with 0.2 N aqueous alcoholic solution of hydrochloric acid.

The yields of products of hydrolysis of the full esters of arylsulfonimidophosphoric acids with a 0.2 N aqueous alcoholic solution of hydrochloric acid are set forth in Table 2.

Short-period boiling of esters of arylsulfonimidophosphoric acids with aqueous alcoholic hydrochloric acid causes the hydrolysis to proceed mainly to the first stage with formation of dialkyl esters according to the scheme:

$$ArSO_2N{=}P(OAlk)_3 + H_2O \xrightarrow{H^{\cdot}} ArSO_2NHPO(OAlk)_2 + AlkOH.$$

Realization of the second stage of hydrolysis with the aim of obtaining the monoalkyl esters was not possible. Hydrolysis always yielded the arylsulfamides.

Hydrolysis of trialkyl esters of arylsulfonimidophosphoric acids in an alkaline medium proceeds very much more easily and quickly than the hydrolysis of the same esters in an acid medium; in these conditions hydrolysis always leads to salts of the dialkyl esters:

$$ArSO_2N{=}P(OAlk)_3 + NaOH \rightarrow ArSO_2NNa{-}PO(OAlk)_2 + AlkOH.$$

In aqueous solutions of alkali, however, hydrolysis proceeds very slowly, apparently due to the same reason as the slowness of hydrolysis in aqueous solutions of mineral acids, i.e. the poor solubility of the full esters in water.

An exception is the trimethyl ester of phenylsulfonimidophosphoric acid, which when shaken with 1 N aqueous solution of NaOH is wholly converted after only 30 minutes at room temperature into the sodium salt of the dimethyl ester:

$$C_6H_5SO_2N{=}P(OCH_3)_3 + NaOH \rightarrow C_6H_5SO_2NNa{-}PO(OCH_3)_2 + CH_3OH.$$

In aqueous-alcoholic solution of NaOH the hydrolysis proceeds easily and quickly in the case of all the full esters. Thus, on heating on a water bath 0.001 -mole of trialkyl esters of arylsulfonimidophosphoric acids with 0.2 N aqueous alcoholic NaOH (5 ml 1 N aqueous solution of NaOH + 20 ml alcohol), hydrolysis takes place quantitatively in 1 hour.

Neither dilute nor concentrated solutions of alkalies, nor sodium ethoxide, hydrolyze the trialkyl esters beyond the stage of formation of salts of dialkyl esters.

In ths respect trialkyl esters of arylsulfonimidophosphoric acids resemble the esters of monobasic mineral acids, for example triethyl phosphate, diethyl sulfate and diethyl carbonate, which only undergo hydrolysis of one ester group in alkaline solution [3].

Yields of hydrolysis products are set forth in Table 3.

TABLE 3

Yield of Dialkyl Esters of Arylsulfcnamidophosphoric Acids on Hydrolysis of 0.001 -mole of the full Esters with Aqueous-Alcoholic Solution of Sodium Hydroxide

Formula of ester subjected to hydrolysis	Yield of dialkyl ester (in g)	Yield of dialkyl ester (in %)	Melting Point
$C_6H_5SO_2N{=}P(OCH_3)_3$	0.26	93.1	108-109°
α-$C_{10}H_7SO_2N{=}P(OCH_3)_3$	0.30	95.1	164-165
β-$C_{10}H_7SO_2N{=}P(OCH_3)_3$	0.29	92.0	144-145
o-$CH_3C_6H_4SO_2N{=}P(OC_2H_5)_3$	0.27	96.7	97-98
α-$C_{10}H_7SO_2N{=}P(OC_2H_5)_3$	0.33	96.1	154-155
β-$C_{10}H_7SO_2N{=}P(OC_2H_5)_3$	0.33	96.1	161-162
α-$C_{10}H_7SO_2N{=}P(OC_4H_9)_3$	0.37	92.5	75-77

On the basis of the observation that trialkyl esters are easily and completely hydrolyzed to dialkyl esters in alkali solutions, it may be suggested that dialkyl esters should be obtainable in good yield directly from trichlorophosphazosulfonaryls if 4 -moles or more of sodium alkoxides and not 3, are introduced into the reaction for each -mole trichlorophosphazosulfonaryl.

Actually, if a benzene solution of 0.01 mole trichlorophosphazosulfonaryl is run with stirring into a solution of sodium alkoxide, taken in excess (0.045 -mole), then the sodium salt of the dialkyl ester is formed according to the scheme:

$$ArSO_2N{=}PCl_3 + 3AlkONa \rightarrow 3NaCl + ArSO_2N{=}P(OAlk)_3,$$

$$ArSO_2N{=}P(OAlk)_3 + AlkONa \rightarrow ArSO_2NNa{-}PO(OAlk)_2 + AlkOAlk.$$

Acidification of the aqueous solutions of the sodium salts of the dialkyl esters brings down the difficultly soluble free dialkyl esters whose properties are identical with those of the dialkyl esters obtained as secondary products in the synthesis of trialkyl esters or in the alkaline hydrolysis of trialkyl esters (see above). The dialkyl esters obtained in this way are set forth in Table 4.

TABLE 4

Yield of Dialkyl Esters of Arylsulfonamidophosphoric Acids when Prepared Directly from 0.01 mole of Trichlorophosphazosulfonaryls

Formula of dialkyl ester	Yield (in g)	Yield (in %)	Melting Point
$C_6H_5SO_2NHPO(OCH_3)_2$	2.37	89.4	108-109°
p-$CH_3C_6H_4SO_2NHPO(OCH_3)_2$	2.27	74.0	110-111
α-$C_{10}H_7SO_2NHPO(OCH_3)_2$	2.91	92.3	164-165
p-$CH_3C_6H_4SO_2NHPO(OC_2H_5)_2$	2.53	82.4	105-106
α-$C_{10}H_7SO_2NHPO(OC_2H_5)_2$	3.07	89.6	154-155

The dimethyl and diethyl esters of arylsulfonamidophosphoric acids are colorless crystalline compounds. In comparison with the full esters they all possess relatively high melting points; they crystallize nicely from water or dilute alcohol. The dimethyl and diethyl esters are readily soluble in acetone, chloroform, dichloroethane, hot alcohol and boiling benzene; the dialkyl esters are difficulty soluble in ether, ligroin, carbon tetrachloride, cold benzene and cold water.

Chemically the dialkyl esters are monobasic acids which displace carbonic and acetic acid from their salts. They titrate with sodium hydroxide to exactly one equivalent (using phenolphthalein as indicator).

The dibutyl esters of arylsulfonamidophosphoric acids are viscous liquids with the exception of the readily crystallizable dibutyl ester of α-naphthylsulfonamidophosphoric acid.

EXPERIMENTAL

Reaction of Trichlorophosphazosulfonaryls with a Solution of Sodium Methoxide in Methyl Alcohol

Into a three-necked flask of 150 ml capacity, fitted with reflux condenser, thermometer and dropping funnel, is introduced 15 ml anhydrous methanol, and addition is made of 0.7 g (0.03 mole) metallic sodium. After all the sodium has dissolved, the reflux condenser is replaced by a stirrer.

The mass is cooled with ice water; with energetic stirring, a solution of 0.01 mole trichlorophosphazosulfonaryl in 30 ml dry benzene is run in at such a speed (20-30 minutes) that the temperature of the reaction mixture does not rise above 5°. When the mixing of the reacting solutions is completed, the sodium chloride is drained off at the pump and washed with methanol. The filtrate is evaporated and the benzene and alcohol are distilled off on a boiling water bath. The residue is a viscous, oily liquid to which is added 30 ml water. After thorough shaking, the sodium salts of the acid esters of the arylsulfonamidophosphoric acids go into solution while the water-insoluble trimethyl esters of arylsulfonimidophosphoric acids generally come down in the crystalline state. The crystal mass is drained off, well washed with water, and recrystallized.

The trimethyl esters of phenyl- and p-tolylsulfonimidophosphoric acids have a relatively low melting point so that treatment of the reaction mixture with water causes them to separate as a heavy oily layer. They are isolated by extraction of the aqueous mixture with benzene. The benzene extract is washed with water, filtered and dried with sodium sulfate; the benzene is driven off in vacuum on a boiling water bath. The residual light-yellow, oily liquid readily crystallizes on cooling with iced water and rubbing with a glass rod.

The yield of full methyl esters of arylsulfonimidophosphoric acids is 70-80%.

If the aqueous solutions are made acid to congo with hydrochloric acid after separation of the full methyl esters, the dimethyl esters of the arylsulfonamidophosphoric acids come down either at once in the crystalline form or, more often, as a heavy, oily layer which easily crystallizes when rubbed with a glass rod. The yield of dimethyl esters is 15-20%.

By this method were obtained the following esters.

Trimethyl phenylsulfonimidophosphate. Yield 2.12 g (75.9%). The crude product was purified by pressing between filter paper and crystallizing from slowly evaporating ethyl ether. Large, well-formed prisms, m.p. 30-40°.

0.0284 g sub.: 1.256 ml N_2 (16°, 742 mm). 0.0336 g sub.: 1.480 ml N_2 (16°, 742 mm). 0.0238 g sub.: 29.60 ml 0.0505 N $Na_2S_2O_3$. 0.0214 g sub.: 27.2 ml 0.0505 N $Na_2S_2O_3$. 0.1532 g sub.; 21.65 g dioxane: Δt 0.130° 0.1202 g substance; 22.32 g dioxane: Δt 0.104°. Found %: N 5.10, 5.08; OCH_3 32.47, 33.19. M 252.0, 239.8. $C_9H_{14}O_5NSP$. Calculated %: N 5.02; OCH_3 33.34. M 279.25.

Trimethyl o-tolylsulfonimidophosphate. Yield 2.23 g (76.0%). Crystallizes from 50% ethanol or from carbon tetrachloride as well-formed prisms, m.p. 74-75°.

0.0248 g sub.: 1.052 ml N_2 (20°, 740 mm). 0.0262 g sub.: 1.120 ml N_2 (20°, 740 mm). 0.0201 g sub.: 24.05 ml 0.0505 N $Na_2S_2O_3$. 0.0234 g sub.: 28.20 ml 0.0505 N $Na_2S_2O_3$. Found %: N 4.81, 4.85; OCH_3 31.23, 31.46. $C_{10}H_{16}O_5NSP$. Calculated %: N 4.77, OCH_3 31.73.

Trimethyl p-tolylsulfonimidophosphate. Yield 2.36 g (80.5%). Stout, transparent, regularly formed prisms (from ether), m.p. 44-45°.

0.0272 g sub.: 32.30 ml 0.0505 N $Na_2S_2O_3$. 0.0227 g sub.: 26.90 ml 0.0505 N $Na_2S_2O_3$. Found %: OCH_3 31.00, 30.94. $C_{10}H_{16}O_5NSP$. Calculated %: OCH_3 31.73.

Trimethyl α-naphthylsulfonimidophosphate. Yield 2.36 g (71.7 %). Colorless, regularly formed prisms (from alcohol or carbon tetrachloride), m.p. 84 -85°.

0.0302 g sub.: 1.080 ml N_2 (14°, 752 mm). 0.0284 g sub.: 1.020 ml N_2 (14°, 752 mm). 0.0322 g sub.: 35.0 ml 0.0505 N $Na_2S_2O_3$. 0.0293 g substance: 31.6 ml 0.0505 N $Na_2S_2O_3$. Found %: N 4.21, 4.23; OCH_3 28.38, 28.16. $C_{13}H_{16}O_5NSP$. Calculated %: N 4.25; OCH_3 28.27.

Trimethyl β-naphthylsulfonimidophosphate. Yield 2.62 g (79.6 %). Crystallizes nicely from carbon tetrachloride in the form of slender, lustrous scales, m.p. 93-94°

0.0294 g substance: 1.068 ml N_2 (16°, 748 mm). 0.0301 g substance: 32.4 ml 0.0505 N $Na_2S_2O_3$. Found %: N 4.22; OCH_3 28.10. $C_{13}H_{16}O_5NSP$. Calculated %: N 4.25; OCH_3 28.27.

Dimethylphenylsulfonamidophosphate. Yield 0.4 g (15.1%). Small, transparent cubes (water), m.p. 108-109°.

0.0260 g substance: 23.35 ml 0.0505 N $Na_2S_2O_3$. 0.4062 g substance: 7.95 ml 0.2046 N NaOH. 0.1055 g substance: 11.28 ml CH_4 (16°, 750 mm). Found %: OCH_3 23.45. Equiv.* 1.06; active H atoms (Terentyev) 1.16. $C_8H_{12}O_5NSP$. Calculated OCH_3 23.41; equiv. 1.00; active H atoms 1.00.

Dimethyl o-tolylsulfonamidophosphate. Yield 0.57 g (20.4%) Stout clusters of prisms (50% alcohol) m.p. 145-146°.

0.0304 g substance: 25.4 ml 0.0505 N $Na_2S_2O_3$. 0.3866 g substance: 6.90 ml 0.2046 N NaOH. 0.0988 g substance: 9.33 ml CH_4 (15°, 749 mm). Found %: OCH_3 21.81. Equiv. 1.02; active H atoms 1.08. $C_9H_{14}O_5NSP$. Calculated %: OCH_3 22.22. Equiv 1.00; active H atoms 1.00.

Dimethyl p-tolylsulfonamidophosphate. Yield 0.25 g (8.95%). Crystallizes nicely from water or dilute ethanol in the form of stout colorless prisms, m.p. 110-111°.

0.0216 g substance: 18.20 ml 0.0505 N $Na_2S_2O_3$. 0.2556 g substance: 4.52 ml 0.2046 N NaOH. Found %: OCH_3 20.00. Equiv. 1.01. $C_9H_{14}O_5NSP$. Calculated %: OCH_3 22.22. Equiv. 1.00.

Dimethyl α- naphthylsulfonamidophosphate. Yield 0.78 g (25%). Crystallizes nicely from ethyl acetate or dilute (50%) alcohol in the form of prisms, m.p. 164-165°.

0.0293 g substance: 1.114 ml N_2 (17°, 752 mm). 0.0202 g substance: 15.10 ml 0.0505 N $Na_2S_2O_3$. 0.3062 g substance: 4.78 ml 0.2046 N NaOH. Found %: N 4.43; OCH_3 19.52. Equiv. 1.01. $C_{12}H_{14}O_5NSP$. Calculated %: N

Dimethyl-β-naphthylsulfonamidophosphare. Yield 0.4 g (12.3%). Crystallizes from water of dilute (50%) alcohol in the form of long, lustrous needles, m.p. 144-145°.

0.0311 g substance: 22.65 ml 0.0505 N $Na_2S_2O_3$. 0.1864 g substance: 3.05 ml 0.2046 N NaOH. Found %: OCH_3 19.01. Equiv. 1.06. $C_{12}H_{14}O_5NSP$. Calculated %: OCH_3 19.69. Equiv. 1.00.

Reaction of Trichlorophosphazosulfonaryls with a Solution of Sodium Ethoxide in Ethanol

The reaction of trichlorophosphazosulfonaryls with a solution of sodium ethoxide was performed by the same procedure as for the reaction with sodium methoxide. The only difference was that the sodium chloride formed in the reaction comes down in a very finely dispersed state and its removal by filtration is extremely difficult, because it either passes through the filter or rapidly clogs it and brings filtration to a standstill. Without separating off the sodium chloride, the reaction mixture is concentrated by driving off the benzene and alcohol in vacuum on a boiling water bath. To the semiliquid mass remaining after elimination of the solvents is added 30 ml water with good stirring. The water-insoluble triethyl esters separate as a heavy, oily layer.

In the case of the triethyl esters of α- and β-naphthylsulfonimidophosphoric acids, the oily layer fairly readily and quickly crystallizes when rubbed with a glass rod. The crystalline portion is drained, washed with water and crystallized.

The triethyl esters of phenyl-, o- and p-tolylsulfonimidophosphoric acids do not crystallize from an aqueous mixture, and therefore they are separated by extracting the aqueous mixture with benzene. The benzene extract is washed with water and dried with sodium sulfate before the benzene is driven off on the water bath to leave a light-yellow, oily liquid. In the case of triethyl o-tolylsulfonimidophosphate this liquid readily crystallizes on cooling with iced water. The triethyl esters of phenyl-and p-tolylsulfonimidophosphoric acids are liquids which do not solidify when cooled with a mixture of snow and salt.

* Here and subsequently using phenolphthalein as indicator.

By this method were prepared the following esters.

Triethyl phenylsulfonimidophosphate. Yield 2.62 g (81.5%). Liquid.

0.0379 g sub.: 38.53 ml 0.05133 N $Na_2S_2O_3$. 0.0266 g sub.: 28.00 ml 0.05133 N $Na_2S_2O_3$. Found %: OC_2H_5 39.17, 40.56 $C_{12}H_{20}O_5NSP$. Calculated %: OC_2H_5 42.08.

Triethyl o-tolylsulfonimidophosphate. Yield 2.75 g (82.1%). Crystallizes from a slowly evaporating ethereal solution in the form of stout, transparent prisms, length 1.5-2 cm, m.p. 35-37°.

0.0341 g sub.: 1.213 ml N_2 (21°, 756 mm). 0.0281 g sub.: 29.65 ml 0.0505 N $Na_2S_2O_3$. Found %: N 4.11; OC_2H_5 39.98. $C_{13}H_{22}O_5NSP$. Calculated %: N 4.18; OC_2H_5 40.32.

Triethyl p-tolylsulfonimidophosphate. Yield 2.64 g (78.7%). Liquid.

0.0333 g sub.: 33.90 ml 0.0505 N $Na_2S_2O_3$. 0.0289 g sub.: 29.43 ml 0.0505 N $Na_2S_2O_3$. Found %: OC_2H_5 38.58, 38.58. $C_{13}H_{22}O_5NSP$. Calculated %: OC_2H_5 40.32.

Triethyl α-naphthylsulfonimidophosphate. Yield 3.21 g (86.4%). Separates from ethanol in the form of regular prisms, m.p. 94-95°.

0.0382 g sub.: 1.292 ml N_2 (20°, 742 mm). 0.0248 g sub.: 23.80 ml 0.0505 N $Na_2S_2O_3$. 0.2106 g sub.; 22.61 g dioxane: Δt 0.126°. Found %: N 3.85; OC_2H_5 36.37. M 342.2. $C_{16}H_{22}O_5NSP$. Calculated %: N 3.77; OC_2H_5 36.39. M 371.38.

Triethyl β-naphthylsulfonimidophosphate. Yield 2.80 g (75.4%). Separates from a slowly evaporating ethereal solution in the form of stout prisms, m.p. 51-52°.

0.0292 g sub.: 0.930 ml N_2 (17°, 748 mm). 0.0236 g sub.: 22.55 ml 0.0505 N $Na_2S_2O_3$. Found %: N 3.63; OC_2H_5 36.22. $C_{16}H_{22}O_5NSP$. Calculated %: N 3.77; OC_2H_5 36.39.

Diethyl phenylsulfonamidophosphate. Yield 0.20 g (6.82%). Readily soluble in hot water. Crystallizes nicely from dilute (50%) ethanol as stout prisms, m.p. 111-112°.

0.0272 g sub.: 21.70 ml 0.0505 N $Na_2S_2O_3$. 0.1003 g sub.: 1.68 ml 0.2046 N NaOH. Found %: OC_2H_5 30.23. Equiv. 1.005. $C_{10}H_{16}O_5NSP$. Calculated %: OC_2H_5 30.73. Equiv. 1.00

Diethyl o-tolylsulfonamidophosphate. Yield 0.3 g (9.76%). Prisms (from 50% alcohol). m.p. 97-98°.

0.0337 g sub.: 26.1 ml 0.0505 N $Na_2S_2O_3$. 0.1545 g sub.: 2.47 ml 0.2046 N NaOH. Found %: OC_2H_5 29.35. Equiv. 1.005. $C_{11}H_{18}O_5NSP$. Calculated %: OC_2H_5 29.33. Equiv. 1.00.

Diethyl p-tolylsulfonamidophosphate. Yield 0.23 g (7.48%). Fine, regularly formed prisms (from water), m.p. 105-106°.

0.0207 g sub.: 15.85 ml 0.0505 N $Na_2S_2O_3$. 0.1232 g sub.: 1.97 ml 0.2046 N NaOH. Found %: OC_2H_5 29.02. Equiv. 1.005. $C_{11}H_{18}O_5NSP$. Calculated %: OC_2H_5 29.33. Equiv. 1.00.

Diethyl α-naphthylsulfonamidophosphate. Yield 0.28 g (8.16%). Best purified by reprecipitation from alkali solution followed by crystallization from ethanol. Stout, regularly formed prisms, m.p. 154-155°.

0.0193 g sub.: 13.35 ml 0.0505 N $Na_2S_2O_3$. 0.4591 g sub.: 6.65 ml 0.2000 N NaOH. 0.1187 g sub.: 9.45 ml CH_4 (16°, 749 mm). Found %: OC_2H_5 26.21. Equiv. 0.994; active hydrogen atoms 1.11. $C_{14}H_{18}O_5NSP$. Calculated %: OC_2H_5 26.25. Equiv. 1.00; active hydrogen atoms 1.00.

Diethyl β-naphthylsulfonamidophosphate. Yield 0.7 g (20.4 %). On crystallization from dilute ethanol (30-40%) it separates as regular, small prisms, m.p. 161-162°.

0.0164 g sub.: 11.30 ml 0.0505 N $Na_2S_2O_3$. 0.1860 g sub.: 2.70 ml 0.2000 N NaOH. Found %: OC_2H_5 26.12. Equiv. 0.997. $C_{14}H_{18}O_5NSP$. Calculated %: OC_2H_5 26.25. Equiv. 1.00.

Reaction of Trichlorophosphazosulfonaryls with a Solution of Sodium n-Butoxide in n-Butyl Alcohol

In a three-necked, 150 ml flask, equipped with reflux condenser, thermometer and dropping funnel, is dissolved 0.7 g (0.031 mole) metallic sodium in 20 ml anhydrous butyl alcohol with heating to 120°. After the whole of the sodium has dissolved, the reflux condenser is replaced by a stirrer.

Then the contents of the flask are cooled to 10° and with energetic stirring a solution of 0.01 mole trichlorophosphazosulfonaryl in 30 ml dry benzene is run in at such a rate that the temperature of the reaction mixture does not rise above 20°. The reaction mixture is heated at 50° for 30 minutes. For separation of the tributyl esters the mixture is evaporated by careful heating in vacuum on a boiling water bath to drive off the

benzene and alcohol. Into the viscous, opalescent liquid residue is run 30 ml water and the mixture is well shaken; it is then extracted with 50 ml ether. The ethereal extract is filtered and dried with sodium sulfate; the solvent is then driven off in vacuum on a water bath, leaving a residue of tributyl ester as a liquid which does not crystallize on cooling to -21°. All these esters possess a faint characteristic odor and have a faint yellow color.

Tri-n-butyl phenylsulfonimidophosphate. Yield 3.45 g (85.1%). Liquid.

0.0311 g sub.: 0.885 ml N_2 (18°, 752 mm). 0.0307 g sub.: 0.852 ml N_2 (18°, 752 mm). Found %: N 3.30, 3.22. $C_{18}H_{32}O_5NSP$. Calculated %: N 3.45.

Tri-n-butyl o-tolylsulfonimidophosphate. Yield 3.72 g (88.7%). Liquid.

d_4^{20} 1.111; n_D^{20} 1.491.

0.0470 g sub.: 1.272 ml N_2 (18°, 752 mm). 0.0409 g sub.: 1.100 ml N_2 (18°, 752 mm). Found %: N 3.14, 3.12. $C_{19}H_{34}O_5NSP$. Calculated %: N 3.34.

Tri-n-butyl α-naphthylsulfonimidophosphate. Yield 3.96 g (86.9%). Viscous liquid.

d_4^{20} 1.141; n_D^{20} 1.530.

0.0468 g sub.: 1.240 ml N_2 (20°, 751 mm). 0.0423 g sub.: 1.050 ml N_2 (20°, 751 mm). Found %: N 3.05, 2.86. $C_{22}H_{34}O_5NSP$. Calculated %: N 3.08.

Tri-n-butyl β-naphthylsulfonimidophosphate. Yield 4.14 g (90.9%). Viscous liquid.

d_4^{20} 1.135; n_D^{20} 1.532.

0.0454 g sub.: 1.180 ml N_2 (20°, 751 mm). Found %: N 2.99. $C_{22}H_{34}O_5NSP$. Calculated %: N 3.08.

Hydrolysis of Full Esters of Arylsulfonimidophosphoric Acids with Alcoholic Hydrochloric Acid

Into a 50 ml flask, fitted with reflux condenser, is introduced 0.001 mole trialkyl ester of arylsulfonimidophosphoric acid and 25 ml 0.2 N alcoholic solution of hydrochloric acid (5.0 ml 1 N aqueous hydrochloric acid and 20 ml alcohol); the mixture is heated to the boil for an hour and the alcohol is driven off from the reaction mixture in the vacuum of a water pump. The residue is neutralized with N NaOH solution until neutral to phenolphthalein, and then the non-hydrolyzed full ester is extracted with 20 ml ethyl ether. The ethereal extract is dried with sodium sulfate and filtered; the solvent is removed in vacuum on a water bath. The aqueous solution after separation of non-hydrolyzed ester is evaporated in vacuum to a volume of about 5 ml and acidified with a few drops of concentrated hydrochloric acid until acid to Congo. The dialkyl esters, which separate from the acidified solution in the form of an oil, readily crystallize when rubbed with a glass rod. The crystalline precipitate is drained and dried. Yields of the hydrolysis products are set forth in Table 2.

The products of hydrolysis were identified from the melting point and titration data. Within the limits of experimental error the melting points and the titration values corresponded to those of the pure substances.

Hydrolysis of Full Esters of Arylsulfonimidophosphoric Acids with an Alcoholic Solution of Sodium Hydroxide

To 0.001 mole full ester of the arylsulfonimidophosphoric acid were added 5 ml of N NaOH solution and 20 ml ethyl alcohol. The mixture was heated to the boil for an hour, after which the alcohol was driven off in vacuum. The residue was a transparent solution and consequently did not contain the full ester. After acidification of the solution with a little conc. hydrochloric acid, the dialkyl ester comes out in the form of a viscous, heavy oil which readily crystallizes on rubbing with a glass rod. The crystalline precipitate is drained, washed several times with water, dried and crystallized. The so-prepared dialkyl esters of arylsulfonamidophosphoric acids have sharp melting points after crystallization, and mixed samples with the corresponding diesters prepared by other methods do not show a depression of melting point. For yields and melting points see Table 3.

Properties and analyses of the dimethyl and diethyl esters have been detailed above.

Di-n-butyl α-naphthylsulfonamidophosphate is a colorless crystalline substance with a remarkably bitter taste. The ester has good solubility in alcohol, acetone and carbon tetrachloride; it is insoluble in water and cold ligroin. It crystallizes from ligroin in the form of fine prisms, m.p. 75-77°.

0.0364 g sub.: 0.0723 ml CO_2; 0.0219 g H_2O. 0.5026 g sub.: 6.20 ml 0.2046 N NaOH. Found %: C 54.16; H 6.73. Equiv. 1.01. $C_{13}H_{20}O_5NSP$. Calculated %: C 54.14; H 6.56. Equiv. 1.00.

Preparation of Dialkyl Esters of Arylsulfonamidophosphoric Acids directly from the Trichlorophosphazosulfonaryls

In a round-bottomed flask, fitted with a reflux condenser and dropping funnel, is placed 30 ml anhydrous methyl or ethyl alcohol, and 1.04 g (0.045 g-atom) metallic sodium is added. When the sodium has dissolved, the reflux condenser is replaced by a stirrer, and 0.01 mole trichloriphosphazosulfonaryl in 30 ml dry benzene is run in with energetic stirring. During this stage the reaction temperature rises to 40-50°. At the end of the reaction the benzene and alcohol are distilled off in vacuum on a water bath. The dry residue is dissolved in 20 ml water and acidified with hydrochloric acid until acid to congo. The dialkyl ester separates in the form of a heavy oil which readily crystallizes when rubbed with a glass rod. The crystalline product is drained, washed several times with small portions of water, dried and crystallized.

For yields of reaction products see Table 4.

The dialkyl esters were identified by their melting points and titration values. Mixed tests with the corresponding dialkyl esters prepared by other methods (see above) did not give a metling point depression.

Preparation and Properties of α- and β-Trichlorophosphazosulfonnaphthyls

Into a round-bottomed flask were introduced 0.150 mole (31.03 g) finely pulverized and thoroughly dried α-naphthalenesulfamide, 0.152 mole (31.7 g) pure phosphorus pentachloride and 35 ml dry carbon tetrachloride. The flask was closed with a reflux condenser whose upper end was connected to a hydrogen chloride absorbent. The mixture was heated on a boiling water bath.

After the solvent had begun to boil, a fairly vigorous evolution of hydrogen chloride started. The reaction mixture gradually became fluid and after 20 minutes it had become completely liquid. Hydrogen chloride evolution ceased after an hour and the reaction came to an end. The flask then contained an amber-colored liquid.

Heating was stopped after the reaction came to an end; 45 ml hot carbon tetrachloride was run in, the upper end of the condenser was closed with a calcium chloride tube and the mixture was left to crystallize. The separated crystalline mass was drained, washed with carbon tetrachloride and dried in vacuum at 80-90°. Yield 48.1 g (93.5%).

α-Trichlorophosphazosulfonnaphthyl does not possess a sharp melting point. At 107-110° it becomes "moist", and at 110-112° it melts to a turbid liquid which finally clarifies at 117°. Subsequent repeated crystallization from carbon tetrachloride or ligroin does not change the melting point.

0.1664 g sub.: 9.52 ml 0.05 N H_2SO_4. 0.1390 g sub.: 8.01 ml 0.05 N H_2SO_4. 1.2928 g sub.: 185.8 ml 0.0989 N NaOH. 0.3822 g sub.: 26.6 ml 0.2046 N NaOH. 0.5545 g substance: 13.23 g benzene: Δt 0.616°. 0.4155 g substance: 13.68 g benzene: Δt 0.444°. Found %: N 4.01, 4.03. Equiv. 4.94, 4.95; M 345, 349. $C_{10}H_7O_2NSPCl_3$. Calculated %: N 4.09. Equiv. 5.00; M 342.5.

β-Trichlorophosphazosulfonnaphthyl is prepared in the same way as the α-compound but the reaction takes place much more slowly (3 to 3.5 hours). It must also be noted that when preparing the β-trichlorophosphazosulfonnaphthyl the heating of the reaction mixture should not be interrupted during the course of the whole reaction. Cooling rapidly results in crystallization of the difficultly soluble β-trichlorophosphazosulfonnaphthyl which envelops the unreacted β-naphthalenesulfamide. On the renewal of the heating, the separated β-trichlorophosphazosulfonnaphthyl does not completely go back into solution and a considerable amount of the β-naphthalenesulfamide remains unreacted.

At the end of the reaction, 50 ml carbon tetrachloride is run in and the mixture is left to crystallize. The crystalline product is washed with carbon tetrachloride and dried in a vacuum on a boiling water bath.

β-Trichlorophosphazosulfonnaphthyl is obtained in the form of a snow-white, crystalline powder melting at 130-132°. Yield 46.3 g (90.1%).

The β-naphthalenesulfamide used in the reaction must be thoroughly ground to a fine powder and well dried. The phosphorus pentachloride does not need to be pulverized since it dissolves readily in hot carbon tetrachloride.

0.1268 g sub.: 7.40 ml 0.05 N H_2SO_4. 0.1784 g sub.: 10.32 ml 0.05 N H_2SO_4. 1.2216 g sub.: 175.8 ml 0.0989 N NaOH. 1.0960 g sub.: 76.1 ml 0.2046 N NaOH. Found %: N 4.09, 4.05. Equiv. 4.946, 4.937. $C_{10}H_7SO_2NPCl_3$. Calculated %: N 4.09. Equiv. 5.00.

α - and β -trichlorophosphazosulfonnaphthyls are colorless and odorless crystalline substances. They are readily soluble in acetone, chloroform, ethyl acetate, benzene and hot carbon tetrachloride; they are sparingly soluble in ether and ligroin..

β -Trichlorophosphazosulfonnaphthyl is less soluble in nearly all solvents than the α -compound. Thus, 100 ml carbon tetrachloride at 19° dissolves 2.25 g α -trichlorophosphazosulfonnaphthyl; in the same conditions 1.39 g β -compound dissolves. In boiling carbon tetrachloride α -trichlorophosphazosulfonnaphthyl dissolves very easily (over 200 g in 100 ml solvent), whereas only about 20 g β -compound dissolves in the same amount of solvent. 100 ml benzene at 19° dissolves 5.7 g β-trichlorophosphazosulfonnaphthyl and more than 20 g of the α -compound. Both compounds are readily soluble in boiling benzene.

The trichlorophosphazosulfonnaphthyls react slowly with cold water, finally forming the corresponding naphthalenesulfamides.

On mixing 1 g (0.003 mole) α - or β -trichlorophosphazosulfonnaphthyl with 50 ml water and leaving the mixture to stand at room temperature, a nearly quantitative yield of the corresponding naphthalenesulfamide is obtained after 3 days. In an alkaline medium, in presence of NaOH, hydrolysis takes place with formation of salts of naphthalenesulfonamidophosphoric acids, α - and β -$C_{10}H_7SO_2NHPO(ONa)_2$. The free acids are readily hydrolyzed. Their sodium salts, however, are extremely stable and do not hydrolyze after prolonged boiling with water.

In an alkaline medium α -trichlorophosphazosulfonnaphthyl hydrolyzes twice as quickly as the β -compound; one of the three chlorine atoms enters with particular facility into reaction with water, alcohol, and ammonia.

If 0.34 g (0.001 mole) α - or β -trichlorophosphazosulfonnaphthyl is added to 50 ml 0.04 N NaOH solution (0.002 mole) at 20°, then energetic stirring causes the alkaline reaction (to phenolphthalein) to disappear in 15 minutes in the case of the α -compound and in 32 minutes in that of the β -compound, and the greater part of the substance goes into solution. If double the amount of NaOH is taken (0.004 mole, 50 ml 0.08 N solution), the color of the indicator disappears in the case of the α -compound in 1 and three-quarter hours and in that of the β -compound in 3 and three-quarter hours.

Consequently the first stage of hydrolysis

$$C_{10}H_7SO_2N{=}PCl_3 + H_2O \rightarrow C_{10}H_7SO_2NHPOCl_2 + HCl$$

both for the α - and the β -trichlorophosphazosulfonnaphthyl is seven times as rapid as the second stage in spite of the fact that the first stage takes place in heterogeneous conditions and the second in solution.

On boiling with water the trichlorophosphazosulfonnaphthyls are quickly and completely hydrolyzed with formation of naphthalenesulfamide, hydrogen chloride and phosphoric acid. Neutralization of the acidic products of hydrolysis of trichlorophosphazosulfonnaphthyls with a standard solution of NaOH is a rapid and convenient method of analysis of trichlorophosphazosulfonnaphthyls.

When kept in sealed ampoules or in flasks with a good ground-glass stopper, the trichlorophosphazosulfonnaphthyls can be stored unchanged for an indefinitely long period. When stored in the air or in poorly stoppered flasks, they slowly change and evolve hydrogen chloride due to reaction with moist air.

Like the benzene derivatives, the trichlorophosphazosulfonnaphthyls react energetically with ammonia, amines and alcohols. With phenol the reaction only takes place when heat is applied.

α - and β -trichlorophosphazosulfonnaphthyls decompose completely when heated at atmospheric pressure or in vacuum (down to 0.5 mm) and do not distil. They can be purified by recrystallization from carbon tetrachloride or ligroin. Usually, however, this is unnecessary because perfectly pure substances are obtained when using perfectly pure and dry sulfamide and phosphorus pentachloride, and the products are suitable for any preparative purposes.

SUMMARY

1. A study was made of the reaction between trichlorophosphazosulfonaryls and sodium methoxide, ethoxide and butoxide.

2. A number of new methyl, ethyl and butyl esters of arylsulfonimidophosphoric acids were prepared and their properties described.

3. The products of acidic and alkaline hydrolysis of the full esters of arylsulfonimidophosphoric acids were studied.

4. A series of dialkyl esters of arylsulfonamidophosphoric acids were prepared and their properties described.

5. A method was developed for direct preparation of dialkyl esters of arylsulfonamidophosphoric acids from alkoxides and trichlorophosphazosulfonaryls.

6. The synthesis and properties of α- and β-trichlorophosphazosulfonnaphthyls are described.

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SYNTHESIS OF SOME N-OXIDES OF PHENAZINE DERIVATIVES

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The pigment iodinin isolated from Chromobacterium iodinum is 1,5-dihydroxyphenazine-N, N'-dioxide (I) [1]*. This pigment exerts bacteriostatic action on various forms of bacteria [2] in a similar manner to other natural phenazine pigments - pyocyanine (II) and chlororaphine (III) [3].

This greatly stimulated interest in the chemistry of phenazine compounds, particularly the hydroxy derivatives and the N-oxides of phenazine. Here we must refer readers to publications in recent years by A.I. Kiprianov, and his co-workers, S.B. Serebryany, V.P. Chernetsky and others, who have greatly enriched our knowledge in the field of the chemistry of phenazine and its derivatives [1, 5-11].

Continuing our studies in the field of phenazine derivatives [4, 12-14], we were interested in the N-oxides of phenazines and in particular in the N-oxides of phenazine-1-carboxylic acid. This acid is the foundation of the molecule of the pigment chlororaphine (III) which is an unusual quinhydrone of the amide of this acid ("hydroxychlororaphine") and its dihydro derivative [4].

On oxidizing phenazine-1-carboxylic acid as well as its amide with hydrogen peroxide in glacial acetic acid, we obtained substances with a bright-orange color whose analysis for nitrogen and whose polarograms identified them as N-monoxides. We may point out that in these conditions of oxidation, phenazine readily gives the N,N'-dioxide (IV), i.e. an oxygen atom here adds on to each nitrogen atom.

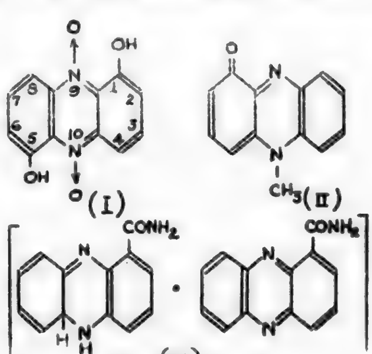
The difficulty of addition of a second oxygen in the case of oxidation of phenazine-1-carboxylic acid and its amide is apparently due to the steric hindrance resulting from the presence of a carboxyl and carboxamido group in the 1-position. It must therefore be postulated that an oxygen atom adds on to the nitrogen remote from the COOH- and $CONH_2$- groups (V, VI).

Similar cases of steric hindrance in the preparation of phenazine N-oxides have also been observed in the past. Thus, 1,2-benzophenazine gives a monoxide of structure (VII) [15]. (Compare also the preparation of monoxides in the oxidation of 1-ethoxyphenazine [10] and 1,5-dichlorophenazine [16]).

The prepared N-oxides are well-crystallizable substances. Phenazine carboxylic acid N-oxide gives a sodium salt which is readily soluble in water and is probably the first stable, water-soluble derivative of phenazine N-oxide.

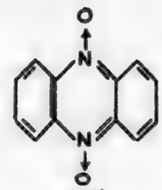
Notwithstanding that the N-oxide of the amide with the structure (VI) contains the skeleton of the antibiotics iodinin (I) and chlororaphine (III), its bacteriostatic action proved to be insignificant and similar to the action of phenazine-1-carboxylic acid and its amide [17, 18, 19].

In addition to the synthesis of the above oxides (V and VI) which are related to chlororaphine, we effected the synthesis of 2,6-dihydroxyphenazine-N,N'-dioxide (XI), an isomer of iodinin (I). Since, however, Vivian's paper [20] on the synthesis of the compound has appeared, we limit ourselves here to a description of a new method of preparation of 2,6-dichlorophenazine (VIII) which we used as an intermediate for the synthesis of the ethoxy derivative (X) and isoiodinin (XI).



2,6-Dichlorophenazine (VIII) was obtained by the action of phosphorus oxychloride on phenazine-N,N'-dioxide (IV). Formation of a chloro derivative by the action of $POCl_3$ on an N-oxide is known, for example, in the case of the N-oxide of quinoline and pyridine [21]; in the case of phenazine N-oxides, this reaction is here applied for the first time (see Experimental). Product (VIII) was identified as the dichloro derivative obtained by Bamberger [22].

* On the numbering system of Chemical Abstracts iodinin is 1,6-dihydroxyphenazine-5,10-dioxide.- Publisher.



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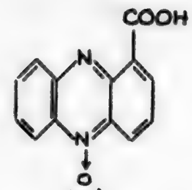

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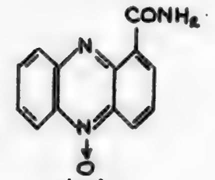

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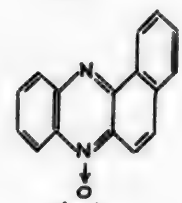

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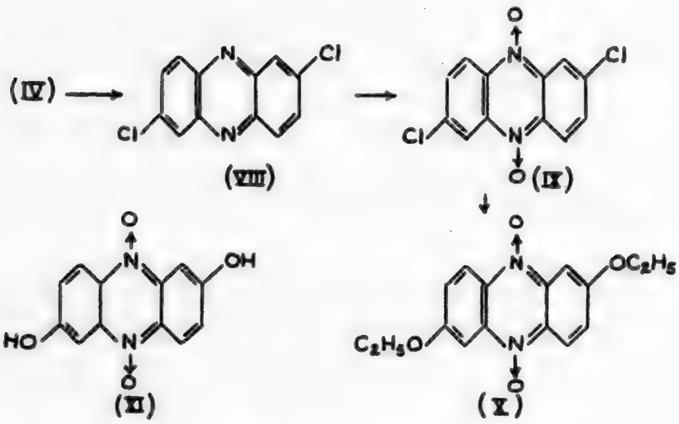

EXPERIMENTAL

1) Phenazine-1-Carboxylic Acid N-oxide

To a solution of 0.5 g phenazine-1-carboxylic acid in 25 ml glacial acetic acid was added 2.5 ml perhydrol (30%); a part of the phenazine-1-carboxylic acid then came down in the form of a fine precipitate. The reaction mass was heated on a water bath at 50-55°. The green precipitate of phenazine-1-carboxylic acid gradually went into solution, and after 1 and one-half to 2 hours a crystalline, bright-yellow precipitate of oxidation product came down. After 10-12 hours' standing at room temperature, the precipitate was filtered, washed with water and dried at 50°. Yield 56%; m.p. 218-219°. Recrystallization from glacial acetic acid yielded fine, bright-yellow needles with a constant m.p. of 223-224°.

4.430 mg sub.: 0.460 ml N_2 (19°, 738 mm). Found %: N 11.80. $C_{13}H_8O_3N_2$. Calculated %: N 11.68.

2) Na Salt of Phenazine-1-Carboxylic Acid N-oxide

0.5 g phenazine-1-carboxylic acid N-oxide was dissolved by heating in 20 ml 2% NaOH solution. The dark solution was filtered hot. On cooling, beautiful yellow platelets of the Na salt of phenazine-1-carboxylic acid N-oxide came down. After recrystallization from water the yield was 55-56%.

3) Phenazine-1-Carboxamide N-oxide

Phenazine-1-carboxamide N-oxide was obtained in a similar manner to the N-oxide of the acid. Yield 47%; m.p. 241-242°. Recrystallization from glacial acetic acid gave bright-yellow needles with a constant m.p. of 249-250°.

4.090 mg sub.: 0.627 ml N_2 (22°, 747 mm). 3.790 mg sub.; 0.568 ml N_2 (20°, 747 mm). Found %: N 17.44, 17.18. $C_{13}H_9O_2N_3$. Calculated %: N 17.57.

4) Action of $POCl_3$ on Phenazine-N,N'-dioxide

2 g N,N'-dioxide was heated at the boil with 40 ml phosphorus oxychloride. At the start the yellow solution gradually darkened to brown.

After 3 hours heating the reaction solution was poured onto ice. The resultant light-brown precipitate was filtered off, washed with water, and then purified by dissolving in conc. HCl. The hydrochloric acid solution was filtered and the product was precipitated by adding ammonia until the reaction was alkaline. The greenish-yellow precipitate was filtered off, washed with water, and dried at 100°. Weight 1.9 g.

The precipitate comprised a mixture of chloro derivatives of phenazine and had the unsharp m.p. of 110-116°.

The mixture was resolved by taking advantage of the differing solubilities of the chloro derivatives in ethanol.

Treatment of the mixture at the boil with 50 ml ethanol caused a part of the precipitate to go into solution. The insoluble portion was filtered off, dried, and crystallized from a mixture of glacial acetic acid and xylene (1:1). Yellow needles separated out with m.p. 264-265°, identical with the melting point of 2,6-dichlorophenazine (0.05 g).

A mixed sample with the 2,6-dichlorophenol prepared by Bamberger's method [22] melted without depression.

3.110 mg sub.: 0.311 ml N_2 (20°, 751 mm). Found %: N 11.53. $C_{12}H_6N_2Cl_2$. Calculated %: N 11.25.

From the mother liquor after distillation of the ethanol and four recrystallizations of the residual product from ethanol was isolated a substance with m.p. 175°. Weight 0.08 g. This proved identical with 2-chlorophenazine-N-oxide prepared by condensation of p-nitrochlorobenzene with aniline in presence of KOH.

4.840 mg sub.: 0.519 ml N_2 (24°, 734 mm). Found%. N 11.90. $C_{12}H_7ON_2Cl$. Calculated %: N 12.15.

Action of $POCl_3$ on Phenazine-N-oxide

2 g phenazine-N-oxide was heated for 3 hours with 40 ml $POCl_3$ at the boil. The phenazine-N-oxide dissolved nicely in the $POCl_3$ to a light-yellow solution which darkened on heating. After 3 hours heating the solution was poured onto ice, when a yellow precipitate came down with m.p. 108-110°. Weight 1.6 g.

Recrystallization from ethanol gave yellow needles of 2-chlorophenazine with m.p. 138° (literature data: 138°) [23]. Weight 0.3 g.

A mixed test with 2-chlorophenazine obtained by condensation of p-chloroaniline with nitrobenzene by Wohl's method did not give a melting point depression.

SUMMARY

1. It is shown that oxidation of phenazine-1-carboxylic acid and its amide with hydrogen peroxide leads to the monoxides (V and VI). Apparently the presence of the carboxyl or the carboxamido group in the 1-position hinders the addition of a second oxygen atom to the nitrogen atom (in the 9-position).

2. A new example of formation of chloro derivatives of phenazine by the action of $POCl_3$ on phenazine N-oxides is described.

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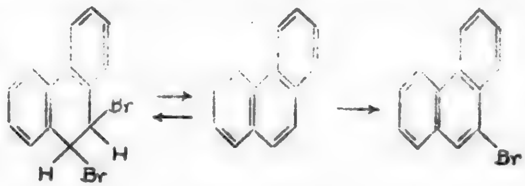
IMIDAZOLE DERIVATIVES

XIII. BROMINATION OF 1,2-NAPHTHIMIDAZOLE [1]

L. S. Efros, L. N. Kononova, and Ya. Eded

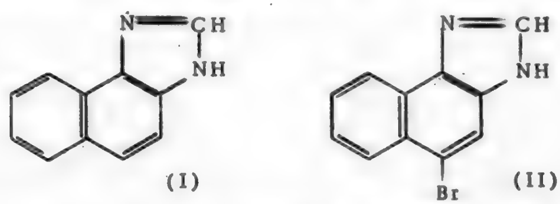
In the preceding communication[1] it was shown that in accord with our theoretical considerations on the character of the influence of the imidazole ring on disturbance of equivalence of bonds in molecules containing condensed rings, 1,2-naphthimidazole (I) behaves like phenanthrene on oxidation.

Extremely characteristic of phenanthrene is also the reaction with bromine which, in addition to smooth formation of the substitution product (the 9-bromo derivative), leads to addition of a bromine molecule at the 9,10- unsaturated bond with formation of a labile product which for a long time was erroneously regarded as an intermediate product of bromination[2]:



It therefore appeared of interest to study the bromination of 1,2-naphthimidazole (I) and thereby continue the comparison of this substance with phenanthrene.

It was found that bromination of 1,2-naphthimidazole proceeds in mineral acid aqueous solutions, in solvents like methyl alcohol and glacial acetic acid, and (most quickly) in an aqueous alkaline medium. In all the product of bromination that we isolated was a monobromo derivative – 4-bromonaphthimidazole (II)*:



(I) (II)

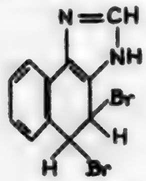
The structure of the bromination product was confirmed by its synthesis from 4-bromo-1,2-naphthylalendiamine, as described under Experimental. For the second part of the research – study of the addition of bromine to 1,2-naphthimidazole – we decided, as in the case of phenanthrene, to conduct this reaction in glacial acetic acid in which the substitution reaction, as we established, proceeds fairly slowly. Actually when the reaction is carried out in sufficiently concentrated solutions, the addition of bromine is followed by separation from the solution of a faint-yellowish substance in the form of fine needles which had an odor of bromine and on heating to 100-120° evolved hydrogen bromide and became colorless. The elementary analysis revealed the presence of two bromine atoms. The compound had good solubility in methanol and ethanol and dissociated in them with loss of bromine. Titration of this free bromine showed that it amounted to 25.7 % of the total bromine content of the compound. Consequently the bromination product obtained in these conditions contained about 25% of the product of addition of bromine to 1,2-naphthimidazole and about 75% of the hydrobromide of 4-bromo-1,2-naphthimidazole (II). The latter was isolated from this product and after purification was found to be identical with the product described above.

In attempting to improve the conditions of formation of the bromine addition product, we effected the bromination in a mixture of carbon tetrachloride and glacial acetic acid at 0° and under irradiation.

* The compound would be the 5-bromo derivative according to Chemical Abstracts numbering – Publisher.

Determination of the amount of bromine split off from the reaction product on dissolving in methanol showed that the product of addition of bromine to 1,2-naphthimidazole represented about 40% of the obtained substance while the product of bromination (II) was present to the extent of about 60%.

Consequently two processes take place simultaneously during the bromination of 1,2-naphthimidazole in the described conditions: formation of a substitution product (II) and formation of an addition product with the probable structure of (III).



(III)

In the light of the above data, the latter substance is much less stable than the analogous product obtained from phenanthrene. On the other hand, the substitution reaction when bromine acts upon 1,2-naphthimidazole also proceeds with considerably greater facility than the bromination of phenanthrene.

It was evidently for these reasons that we failed to select those conditions which would have enabled us to obtain the pure product of addition of bromine to the 1,2-naphthimidazole molecule. Nevertheless a definite similarity between the behavior of 1,2-naphthimidazole and phenanthrene on bromination was established by the above-described experiments.

EXPERIMENTAL

1. 4-Bromo-1,2-naphthimidazole.

a) Bromination of 1,2-naphthimidazole. 5 g 1,2-naphthimidazole is dissolved in 500 ml KOH; after 30 minutes 5 g bromine in 100 ml 1 N KOH is run in. With progressive addition of the Br, a colorless reaction product separates as fine needles. It is washed with water, and dried. Yield 8.1 g, m.p. 272°. After crystallization from dilute acetic acid, m.p. 274°.

0.1147 g substance: 0.0887 g AgBr. 0.1125 g substance; 0.0855 g AgBr. 0.0995 g substance: 9.9 ml N_2 (23°, 750 mm). Found%: Br 32.34, 32.9; N 11.32. $C_{11}H_7N_2Br$. Calculated %: Br 32.35; N 11.2.

b) Condensation of 4-bromo-1,2-naphthalenediamine [3] with formic acid. 2 g 4-bromo-1,2-naphthalenediamine is heated in a flask with a reflux condenser for 3 hours with 15 ml anhydrous formic acid. The reaction mass is diluted with 40 ml 5% hydrochloric acid, boiled for five minutes, and filtered from dirt. The filtrate is neutralized with ammonia and the reaction product collected; after several crystallizations from acetic acid, m.p. 274°; no depression in admixture with the product of bromination of 1,2-naphimidazole. Yield 1 g.

2. Product of Addition of Bromine to 1,2-Naphthimidazole

a) 1 g naphthimidazole is dissolved in a mixture of 25 ml glacial acetic acid and 25 ml carbon tetrachloride. At 20° addition is made to the solution of 0.816 g bromine in 3 ml carbon tetrachloride. Yellow crystals (needles under the microscope) rapidly settle out from the solution. They are filtered, thoroughly washed with carbon tetrachloride and dried in a vacuum-desiccator over paraffin wax.

The compound gives off bromine on heating (test with starch-iodide paper) and at 100-120° it evolves hydrobromic acid (test with congo paper). It splits off bromine when dissolved in methanol or ethanol.

0.1412 g sub.: 10.9 ml N_2 (21°, 742 mm). 0.1033 g sub.: 0.1181 g AgBr. 0.1325 g sub.: 0.1500 g AgBr. Found %: N 8.7; Br 48.6, 48.2 $C_{11}H_8N_2Br_2$. Calculated %: N 8.5; Br 48.7.

0.50 g of the substance is dissolved at 20° in 50 ml methanol and the resultant solution is titrated in a hydrochloric acid medium with 0.098 N sodium thiosulfate in presence of potassium iodide. The titration consumes 8.0 ml thiosulfate, equivalent to 25.7% of the total bromine content of the product. The same result is obtained if the substance is dissolved in methanol at 0°.

b) An experiment is performed as described in section a) but with the difference that it is run at 0° in direct sunlight. 0.5 g of the resultant product is likewise dissolved in methanol at 0° and at 20° and titrated with sodium thiosulfate. In both cases 12.1 ml thiosulfate is consumed, equivalent to 38.5% of the total bromine of the substance.

SUMMARY

1. The known similarity between 1,2-naphthimidazole and phenanthrene, previously demonstrated [1] in a study of the oxidation of 1,2-napthimidazole, is also manifested in the bromination of this compound. The latter reaction, as in the case of phenanthrene, proceeds in two directions – with formation of a 4-substituted product and of a labile and easily dissociated product of addition of a molecule of bromine to the 1,2-naphthimidazole molecule.

2. These characteristics of 1,2-naphthimidazole find their explanation by our previously expounded [4] ideas of the nature of the influence of the imidazole ring on the disturbance of the equivalence of bonds in molecules containing condensed rings.

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EMPLOYMENT OF ANTIMONY PENTACHLORIDE IN THE GUSTAVSON–FRIEDEL-CRAFTS REACTION

A.M. Petrova

The employment of antimony pentachloride in the Gustavson–Friedel-Crafts reaction has not received adequate consideration in the literature.

We carried out a number of experiments to compare $SbCl_5$ with the classic catalyst for this reaction ($AlCl_3$) as well as with $SnCl_4$.

All the experiments were performed with benzene, to which were added:

1) Halogeno derivatives in the shape of primary halogenated butanes and benzyl chloride and 2) carboxylic acid chlorides and ethyl nitrate.

Experiments with esters have been described previously [1].

Of the halogenated hydrocarbons that we tested, only benzyl chloride reacted with benzene in presence of $SbCl_5$, but the yield of diphenylmethane was lower than in the case of $AlCl_3$. The reaction did not take place with butyl chloride, bromide or iodide. It is interesting, however, that chlorination of benzene was not observed with any of these halogeno derivatives, a process which takes place readily with $SbCl_5$ alone [2]. It must be assumed that the butyl halides form a complex with $SbCl_5$ which does not react with benzene.

In our conditions benzoyl chloride with $SbCl_5$ gave a higher yield of benzophenone than with $AlCl_3$. The yield was 210% ketone calculated on the $SbCl_5$, i.e. in this case the reaction, in contrast to the synthesis with $AlCl_3$, actually possesses a catalytic character. $AlCl_3$ must be taken in equimolecular ratio to the acid chloride since in the reaction a stable complex of ketone with $AlCl_3$ is formed [3]. The complex of $SbCl_5$ with benzophenone is evidently less stable. Due to its decomposition, the $SbCl_5$ is able to convert fresh quantities of benzene and acid chloride into ketone.

On the assumption of a similar mechanism for the reaction of benzene with esters, we attempted to isolate the binary and ternary complexes in experiments with ethyl nitrate. These attempts failed completely with $AlCl_3$ and $SnCl_4$. On evaporation of solutions of $AlCl_3$ and $SnCl_4$ in excess of $C_2H_5ON_2$, decomposition takes place even at temperatures below 0°. In the former case oxides of nitrogen are evolved; in the latter case $SnCl_4$ distils off.

On adding $SbCl_5$ to ethyl nitrate there is an immediate detonation. On mixing $SbCl_5$ with ethyl nitrate in carbon tetrachloride, however, separation of a viscous, dark blue liquid is observed at a temperature of about −20°; this liquid may be assumed to be the anticipated complex. Addition of benzene to this substance gives nitrobenzene.

The yield of the latter rises if more ethyl nitrate is added.

EXPERIMENTAL

Into a three-necked flask, fitted with a mercury-sealed stirrer, a dropping funnel and a reflux condenser, is introduced 0.5 mole halogenated hydrocarbon or acid chloride and 2 moles benzene. From the dropping funnel is added 0.125 mole $SbCl_5$ with cooling and stirring. To the dropping funnel was attached a calcium chloride tube. Another calcium chloride tube was fixed to the end of the condenser and joined to a tube whose end dipped into a cylinder of water for absorption of the evolved gases. The mixture was heated at 70° for 4 hours on a water bath; the $SbCl_5$ was then decomposed with water and the hydrocarbon portion was steam distilled. The residue was extracted with ether. The benzene-ether layer was dried with calcium chloride and fractionated.

The results of the experiments are set forth in the table.

Alkylated or acylated substance	Reaction product	Yield of product on basis of catalyst used (in %)	
		$SbCl_5$	$AlCl_3$
Benzyl chloride.	Diphenylmethane	35	46.8
Benzoyl chloride.	Benzophenone	72	21.7
Acetyl chloride.	Acetophenone	0.5	0.8
Butyl bromide	sec-Butylbenzene	6	38.8
	n-Butylbenzene	0	13.1
Butyl iodide	sec-Butylbenzene	0	41.8
	n-Butylbenzene	0	9.7
Butyl chloride	sec-Butylbenzene	3	28.3
	n-Butylbenzene	0	25.4

Reaction of Ethyl Nitrate with $SbCl_5$

To a solution of 0.125 mole $SbCl_5$ in carbon tetrachloride, cooled to −21°, was added dropwise at the same temperature 0.5 mole ethyl nitrate in carbon tetrachloride. After 30 minutes a heavy, dark blue oily layer separated. After separation and washing of the lower layer with carbon tetrachloride, 2 moles of benzene was run into each layer. The wash liquor was added to the top layer. The whole was left for 3 hours and then heated for 2 hours on a water bath; it was then decomposed with water; the hydrocarbon layer was dried with $CaCl_2$ and fractionated. The upper layer contained 5.53% $C_6H_5NO_2$ and the lower layer 5.72% reckoned on the ester.

In order to check whether the complex acts as a catalyst, repeated washings with carbon tetrachloride were followed by addition of another 0.5 mole ethyl nitrate and 2 moles benzene. Heating and working-up were conducted as described above. After fractionation the upper layer contained 3.9% $C_6H_5NO_2$ (36.6% Sb) and the lower layer 16% $C_6H_5NO_2$ (63.7% Sb).

Carbon tetrachloride slightly retards ring substitution. Thus in experiments without carbon tetrachloride, 35.5% nitrobenzene was obtained, while in carbon tetrachloride solution the yield of nitrobenzene was only 27%.

SUMMARY

1. A comparison was made of the catalytic action of $AlCl_3$ and $SbCl_5$ in reactions of benzene with some halogenated hydrocarbons, carboxylic acid halides, and ethyl nitrate.

2. It was established that in the reaction with halogenated hydrocarbons antimony pentachloride acts much less intensively than aluminum chloride.

3. In the reaction of benzene with some acid halides, antimony pentachloride is a good catalyst; in contrast to the action of aluminum chloride, the process is actually a catalytic one.

4. Antimony pentachloride was also a good catalyst in the reaction with ethyl nitrate. In this case the formation could be observed of an unstable compound of $SbCl_5$ with $C_6H_5NO_2$. This compound is an intermediate product of reaction on the one hand and may catalyze the reaction of benzene with a fresh quantity of ethyl nitrate on the other hand.

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EPOXY ALCOHOLS (OXIDOLS)

III. PREPARATION AND PROPERTIES OF 2,3-EPOXY-2-METHYL-4-BENZYL-4-PENTANOL

V.I. Pansevich-Kolyada and V.A. Ablova

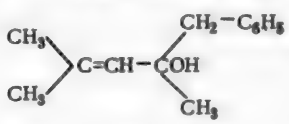
Previous investigations [1, 2] of α,β-epoxy alcohols showed that the properties of the oxide ring of these compounds sharply differed from those of the oxide ring of α-oxides of olefinic hydrocarbons.

Reaction of acetic anhydride with α,β-epoxides of the aliphatic series resulted in acetylation at the hydroxyl group with retention of the oxide ring; heating with fused zinc chloride of α,β-epoxy alcohols caused cleavage into aldehydes and ketones instead of isomerization into carbonyl compounds.

The epoxy alcohol 2,3-epoxy-2-methyl-4-phenyl-4-petnanol [1], containing a phenyl radical at the tertiary alcoholic group, split into acetophenone and isobutyraldehdye even without the action of any reagents when kept in a desiccator over sulfuric acid, calcium chloride or phosphorus pentoxide, and also in dilute sulfuric acid and when heated.

The cause of the special instability of the oxide 2,3-epoxy-2-methyl-4-pentanol was evidently the great accumulation of electronegative groups at the 2, 3 and 4 carbon atoms of the compound. In order, therefore, to obtain a more stable phenyl-containing epoxide, it is evidently necessary to have a certain distance between these groups. As a test of this hypothesis we realized the preparation of the epoxy alcohol 2,3-epoxy-2-methyl-4-benzyl-4-pentanol (I) by oxidation of 2-methyl-4-benzyl-2-penten-4-ol with acetyl hydroperoxide.

We synthesized the alcohol, in a similar manner to Fellenberg [3], by the Grignard reaction from benzylmagnesium chloride and mesityl oxide. It should be noted that, contrary to the categorical assertion of Esafov [4] regarding the absence of normal reaction between benzylmagnesium chloride and mesityl oxide, we obtained 2-methyl-4-benzyl-2-penten-4-ol (II) by this reaction in a yield of up to 60% of the theoretical



(II)

Oxidation of this alcohol was conducted in a solution of anhydrous ether with 65% acetyl hydroperoxide. The products of oxidation partly crystallized. The isolated crystalline substance had m.p. 71.5-72.5°. It was the epoxy alcohol, 2,3-epoxy-2-methyl-4-benzyl-4-pentanol (I).

The latter forms white crystals with a camphor-like odor; unlike, 2,3-epoxy-2-methyl-4-phenyl-4-pentanol, it did not change when kept in a desiccator over sulfuric acid. Heating with acetic anhydride yielded the oxido-acetate with m.p. 121-122°. Acetylation took place at the hydroxyl group with retention of the oxide ring, as in the case of the previously studied alcohol-oxides of the aliphatic series [2].

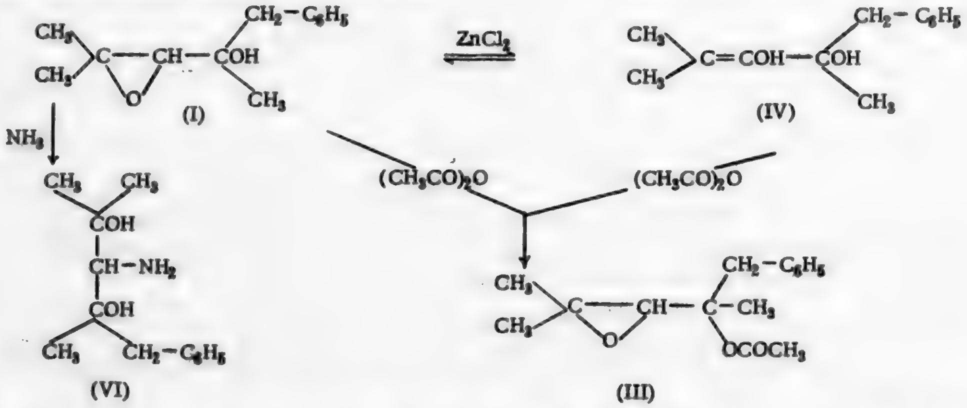
Heating of 2,3-epoxy-2-methyl-4-benzyl-4-pentanol (I) with anhydrous zinc chloride or even with extremely dilute aqueous sulfuric acid led to formation of a substance with m.p. 138-139°.

The quantitative composition of this substance and the epoxy alcohol was the same and corresponded to the formula $C_{13}H_{18}O_2$. Consequently it was a product of isomerization of the epoxy alcohol under the action of fused zinc chloride and dilute sulfuric acid. The substance with m.p. 138-139° did not contain a carbonyl group but contained two hydroxyl groups. This is only possible if our epoxy alcohol had isomerized not to a ketoalcohol but to an unsaturated glycol whose structure most probably corresponds to 2-methyl-4-benzyl-2-penten-3,4-diol (IV).

The same substance was obtained also on vacuum distillation of the mother liquor of the non-crystallizable products of oxidation which remained after separation of the alcohol-oxide.

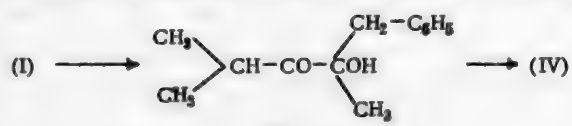
Heating of the unsaturated glycol (IV) with acetic anhydride yields the oxidoacetate (III) with m.p. 121-122°, identical with the product from the epoxy alcohol in the same conditions.

Consequently, the epoxy alcohol – 2,3-epoxy-2-methyl-4-benzyl-4-pentanol (I) – and the isomeric glycol – 2-methyl-4-benzyl-2-penten-3,4-diol (IV) – are individual chemical compounds capable in suitable conditions of mutual transformations with rupture and reduction of the oxide ring. This extremely interesting and previously unobserved phenomenon evidently points to the occurrence of a new form of oxide-enol tautomerism. Both tautomers give one and the same monoacetate (III):



The new tautomeric transformation differs from those previously known in that the enolic form is formed by translocation of hydrogen atom to an oxygen atom not from an adjacent carbon atom but from the one linked to an oxygen atom.

Formation of the unsaturated glycol (IV) may be represented by the following scheme:



(V)

However, the absence of reactions of the obtained compounds (III and IV) for the carbonyl group and the undoubtedly greater stability of the keto group compared with that of the oxide ring and the hydroxyl group at the double bond are weighty evidence against this scheme.

On heating the epoxy alcohol (I) in a sealed glass tube with aqueous ammonia, an aminodiol is obtained. Krasusky [5] showed that in the formation of aminoalcohols from α-oxides and ammonia, the amino group is usually located at the more hydrogenated carbon atom. Hence the aminoalcohol that we prepared is most probably 2-methyl-4-benzyl-3-amino-2,4-pentanediol (VI).

The present investigation of 2,3-epoxy-2-methyl-4-benzyl-4-pentanol (I) shows that the properties of α,β-epoxy alcohols are determined not only by the presence and position of their functional groups but also by the radicals attached to the oxidized carbon atoms. Remoteness of the phenyl radical from the tertiary alcohol group stablizes the carbon skeleton of the epoxy alcohol (I), in which respect it differs both from epoxy alcohols of the aliphatic series and from the epoxy alcohol, 2,3-epoxy-2-methyl-4-phenyl-4-pentanol, in which the phenyl radical is attached directly to the carbon atom of the tertiary alcohol group. Unlike this epoxy alcohol, the epoxy alcohol (I) did not undergo modification when kept in a desiccator over sulfuric acid, while it was not cleaved under the action of anhydrous zinc chloride as was the case with epoxy alcohols of the aliphatic series, but was only isomerized to the unsaturated glycol (IV). With ammonia the epoxy alcohol (I), like α-oxides of the olefinic hydrocarbons, forms an aminodiol (VI). Finally, due to the stabilization of the carbon skeleton of the α,β-epoxy alcohol (I), it was possible to establish interesting intramolecular transformations. These tautomeric transformations are possibly also characteristic of other epoxy alcohols, but due to the instability of their molecules they apparently proceed at such a velocity that their observation is greatly hindered.

EXPERIMENTAL

Preparation of 2-methyl-4-benzyl-2-penten-4-ol (II)

To 6 g magnesium in anhydrous ether was slowly added 31.6 g benzyl chloride. After heating for an hour, the mixture was cooled and dropwise addition was made of 24.5 g mesityl oxide with cooling. An energetic reaction took place. After addition of the whole amount of mesityl oxide, the mixture was heated for an hour on a water bath and then left overnight. The magnesium complex was decomposed at first with ice and then with saturated NH_4Cl solution. The ethereal solution of the reaction products was dried with potassium carbonate, the ether was driven off, and the alcohol was distilled in vacuum:

b.p. 120-122° at 9 mm; n_D^{20} 1.5186; d_4^{20} 0.9645; MR_D 59.75; calculated 59.69.

0.1543 g sub.: 0.4646 g CO_2; 0.1310 g H_2O. Found %: C 82.16; H 9.50. $C_{13}H_{18}O$. Calculated %: C 82.10; H 9.47.

Oxidation of 2-methyl-4-benzyl-2-penten-4-ol with acetyl hydroperoxide

To 62 g alcohol (II) in 130 ml anhydrous ether was slowly added 39 g 65% acetyl hydroperoxide. Oxidation proceeded quietly without much heat development. The temperature of the mixture was held at 20-25°.

The next day the reaction mixture contained 0.44 g unreacted acetyl hydroperoxide. The acetic acid was neutralized first with sodium carbonate solution and then with dry sodium carbonate. The ethereal solution was dried over $MgSO_4$. After removal of the ether in vacuum, crystallization commenced. 17 g of white crystalline substance with a camphor-like odor was obtained with m.p. (after recrystallization from ethanol) of 71.5-72.5°. The substance was soluble in benzene, isomyl ether, and methyl and ethyl alcohols. It displaced iodine from potassium iodide in acetic acid solution.

0.1331 g substance: 0.3702 g CO_2; 0.1059 g H_2O. 0.1255 g substance: 15.8 ml CH_4 (0°, 760 mm). 0.1204, 0.2134 g substance: 17.39 g benzene: Δt 0.179, 0.312°. Found %: C 75.90, H 8.91; OH 9.60; M 198.8, 201.2. $C_{13}H_{18}O_2$. Calculated %: C 75.75; H 8.74; OH 8.20; M 206.

The liquid portion of the oxidation products was distilled at 5 mm to give the following fractions: 1st frac. b.p. 104-115°; 2nd b.p. 115-119°; 3rd b.p. 119-122°; 4th b.p. 122-130°; 5th b.p. 133-152°.

The second fraction crystallized completely. After recrystallization from ethanol it formed white, fluffy needles with m.p. 138-139°.

0.1370 g sub.: 0.3779 g CO_2; 0.1127 g H_2O. 0.0621 g sub.: 14.28 ml CH_4 (0°, 760 mm). Found %: C 75.30; H 9.20; OH 17.57. $C_{13}H_{18}O_2$. Calculated %: C 75.75; H 8.74; OH 16.5.

The third fraction partly crystallized. The crystals melted at 71.5-72.5° after recrystallization from ethanol.

Reaction of 2,3-epoxy-2-methyl-4-benzyl-4-pentanol with acetic anhydride

4 g alcohol-oxide (I) and 10 g acetic anhydride were heated for 3 hours on a water bath and were then boiled for 10 hours. The acetic anhydride was distilled off in vacuum and the acetylation product was distilled at 4 mm to give the following fractions: 1st frac. b.p. 85-135°; 2nd frac. b.p. 135-155°, 3rd frac. b.p. 155-157° 2.6 g.

The third fraction crystallized to form fine needles, sparingly soluble in ether and ethanol, readily in benzene. After recrystallization from ethanol they melted at 121-122°. The substance did not give a reaction for the carbonyl group; an impurity containing active hydrogen was present (1.52% calculated on hydroxyl). It displaced iodine from potassium iodide in acetic acid solution.

0.1162 g sub.: 0.3050 g CO_2; 0.0810 H_2O. 0.0948 g sub.: 1908 g benzene: Δt 0.106°. Found %: C 71.63; H 8.09; M 240.9. $C_{15}H_{20}O_3$. Calculated %: C 72.58; H 8.02; M 248.

Action of Sulfuric Acid on 2,3-epoxy-2-methyl-4-benzyl-4-pentanol

1.5 g alcohol-oxide (I) was heated on a water bath with dilute sulfuric acid. At the outset the crystals melted but later crystallized in the form of white, coalescent needles, which after recrystallization from ethanol melted at 138-139°. No depression with the product of treatment with zinc chloride (see below).

Action of zinc chloride on 2,3-epoxy-2-methyl-4-benzyl-4-pentanol

2 g (I) and 0.4 g zinc chloride were heated on a water bath. The alcohol-oxide melted and later the whole mass crystallized. No evolution of volatile substances. The substance is soluble with heating in ethanol, and in the cold the same solution deposits long needles, m.p. 138-139°, sparingly soluble in benzene.

0.1120 g substance: 0.3088 g CO_2; 0.0873 g H_2O. 0.0517 g substance: 10.28 ml CH_4 (0°, 760 mm). 0.0988 g substance: 20.03 g benzene: Δt 0.122°. Found %: C 75.24; H 8.73; OH 15.18; M 207.8. $C_{13}H_{18}O_2$. Calculated C 75.75; H 8.74; OH 16.5; M 206.

Reaction of 2-methyl-4-benzyl-2-penten-3,4-diol with acetic anhydride

To 0.9 g glycol (IV) with m.p. 138-139°, obtained by the action of dilute sulfuric acid on 2-epoxy-2-methyl-4-benzyl-4-pentanol (I), was added 5 g acetic anhydride, and the mixture was heated 2 hours on a water bath and then boiled for an hour on a hotplate. The substance dissolved on heating with acetic anhydride and the color changed to yellow. The next day the acetic anhydride was taken off in vacuum and the residue crystallized. Yield 0.35 g with m.p. 121-122°. A mixed test with compound (III), obtained by the action of acetic anhydride on 2,3-epoxy-2-methyl-4-benzyl-4-pentanol, did not give a depression of melting point.

Reaction of 2,3-epoxy-2-methyl-4-benzyl-4-pentanol with ammonia

2 g alcohol-oxide (I) and 30 ml saturated aqueous ammonia were heated in a sealed glass tube at 90-100° for 6 hours. After driving off the ammonia, the reaction product was extracted with ether and the extract dried over $MgSO_4$. The ether was distilled off and the substance recrystallized from hot hexane. The crystals were slender, fine needles melting at 116-117°. Readily soluble in inorganic acids and organic solvents. Nitrogen and active hydrogen were present.

0.1294 g sub.: 6.98 ml N_2 (0°, 760 mm). 0.0747 g sub.: 20.95 g benzene: Δt 0.083°. 0.0740 g sub.: 29.3 ml CH_4 (0°, 760 mm). Found %: N 6.75; active H 1.78; M 220.8. $C_{13}H_{21}O_2N$. Calculated %: N 6.28; active H 1.79; M 223.

SUMMARY

1. Oxidation of 2-methyl-4-benzyl-2-penten-4-ol with acetyl hydroperoxide gives the oxidol, 2,3-epoxy-2-methyl-4-benzyl-4-pentanol, which with acetic anhydride gives the oxido-acetate, 2,3-epoxy-2-methyl-4-benzyl-4-acetoxy-pentane.

2. Heating of 2,3-epoxy-2-methyl-4-benzyl-4-pentanol with anhydrous zinc chloride or dilute sulfuric acid gave the unsaturated glycol, 2-methyl-4-benzyl-2-penten-3,4-diol. With acetic anhydride this glycol gives the same oxido-acetate as was obtained from the oxide-alcohol.

3. 2,3-Epoxy-2-methyl-4-benzyl-4-pentanol reacts with ammonia to form the aminodiol, 2-methyl-4-benzyl-3-amino-2,4-pentanediol.

4. The epoxy alcohol and the unsaturated glycol are individual substances capable of undergoing mutual transformations in appropriate conditions with rupture and reduction of the oxide ring. This transformation may be described as oxido-enol tautomerism.

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** " " " " p. 21.

COMPOUNDS CONTAINING A THREE-MEMBERED OXIDE RING

XI. REACTION OF ETHYL β-METHYL-β-ETHYLGLYCIDATE WITH o- AND p-TOLUIDINE

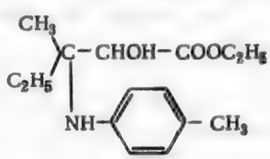
V.F. Martynov and Ya. A. Kastron

In one of the previous communications [1] we described the reaction of ethyl β-methyl-β-ethylglycidate with aniline.

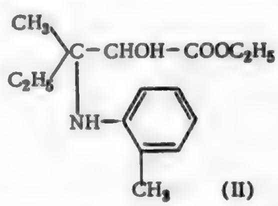
Our present investigation is a continuation of this research. Addition of p-toluidine to the above-mentioned ester of glycidic acid was effected in the usual manner, i.e. by heating the mixture of reactants in a sealed ampoule at 170-180°. The reaction product was obtained in sufficiently good yield. This method proved less suitable, however, for o-toluidine. Steric hindrance, due to the methyl group of o-toluidine, caused the reaction to proceed with difficulty. 50 hours heating in the above-mentioned conditions completely failed to yield the anticipated reaction product.

It must be pointed out that in similar conditions the reaction between o-toluidine and ethyl β,β-ethylglycidate took place with a good yield, [2]. In order to effect the addition of o-toluidine to ethyl-β-methyl-β-ethyl glycidate, we resorted to more drastic conditions. The mixture of components (excess of o-toluidine) was heated to the boil over Wood's alloy in a flask fitted with a reflux condenser protected against atmospheric moisture by a Tishchenko flask containing sulfuric acid. During the process the temperature rose to approximately 200° (the b.p. of o-toluidine). But even in these conditions after 10 hours' heating we obtained a very low yield (11%) of addition product. And only after 22 hours' heating did the reaction proceed with a fully satisfactory yield.

On the basis of all the preceding studies we can ascribe to both products the structure of the ethyl ester of α-hydroxy-β-(o,p-toluidino)-isocaproic acid.

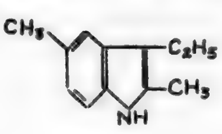


(I)

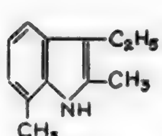


(II)

With the objective of conclusively demonstrating the structure of both of the products that we prepared (I and II), we subjected them to the action of conc. sulfuric acid. As had been expected, evolution of carbon monoxide was observed and conclusively showed that we were indeed dealing with α-hydroxy-β-amino acids. The fragments of the molecules after splitting-off of carbon monoxide should be stablized by transformation into the corresponding indole homologs; on the basis of the preceding investigation [1], it was to be expected that the ethyl ester of α-hydroxy-β-(p-toluidino)-isocaproic acid (I) would after loss of carbon monoxide be transformed into 2,5-dimethyl-3-ethylindole (III), while the ethyl ester of α-hydroxy-β-(o-toluidino)-isocaproic acid should give 2,7-dimethyl-3-ethylindole (IV):



(III)



(IV)

We actually obtained substances the data for which corresponded with the above-mentioned indole homologs. The compound to which we attributed the structure (III) formed colorless, scaly crystals which deliquesced and darkened after a few days. Compound (IV) formed a colorless liquid which darkened relatively quickly in the air.

For conclusive proof of their structure we synthesized 2,5-dimethyl-3-ethylindole by A.E. Arbuzov's method [3] and obtained the same scaly crystals with the same melting point which darkened and deliquesced after a few days. The picrate of the authentic 2,5-dimethyl-3-ethylindole melted at the same temperature as the picrate of the compound that we prepared. No melting point depressions were observed in mixed tests either with the compounds themselves or their picrates. Consequently the structure of compound (III) can be said to be conclusively demonstrated. Concerning compound (IV), we may claim on the basis of our previous investigation [1] and of the foregoing data that its structure undoubtedly corresponds to 2,7-dimethyl-3-ethylindole.

EXPERIMENTAL

Ethyl α-hydroxy-β-(p-toluidino)-isocaproate

40 g ethyl β-methyl-β-ethylglycidate in admixture with 27 g freshly distilled p-toluidine (molar ratio) was heated in a sealed ampoule for 25 hours at 170-180°. The reaction mass was a viscous, light-yellow liquid. Vacuum distillation at 3 mm gave a fraction with b.p. 149-153° in the form of a very viscous, light-yellow liquid which rapidly crystallized; yield 37 g (55 %).

Three recrystallizations from ligroine gave a colorless, finely crystalline powder with m.p. 57-58°.

0.2187 g sub.: 10.1 ml N_2 (21°, 760.6 mm); 0.3948 g sub.: 18.5 ml N_2 (20°, 744.1 mm). Found %: N 5.32, 5.28. $C_{15}H_{23}O_3N$. Calculated %: N 5.28

Synthesis of 2,5-dimethyl-3-ethylindole

5.5 g ethyl α-hydroxy-β-(p-toluidino)-isocaproate was introduced into 35 ml conc. sulfuric acid and heated over a bare flame. Mutual solution of the substances occurred with progressive heating and the liquid acquired a straw-yellow color. At 85° (thermometer in reaction mixture) bubbles of carbon monoxide started to come off and this process became very intensive at 115°. As soon as carbon monoxide evolution had ceased, the reaction mass (without preliminary cooling) was poured into iced water; scaly crystals separated and were collected, washed with water and recrystallized from aqueous ethanol. Light-yellow scales with m.p. 65-66° were obtained. The yield was nearly quantitative.

0.1361 g sub.: 9.8 ml N_2 (20°, 750.3 mm). 0.0787 g sub.: 5.7 ml N_2 (20°, 750.8 mm). Found %: N 8.13, 8.18. $C_{12}H_{15}N$. Calculated %: N 8.09.

The picrate formed dark-red needles with m.p. 144-145° after recrystallization from aqueous ethanol.

Synthesis of 2,5-dimethyl-3-ethylindole by Arbuzov's method

The p-tolylhydrazone of methylpropyl ketone was first prepared. This was a liquid with b.p. 120-122° at 2 mm. To 8 g methylpropyl ketone p-tolylhydrazone was added a trace of powdered zinc chloride. The reaction commenced without heating and was very energetic. The reaction mixture was poured into cold water; an oily layer floated to the surface and quickly crystallized. The crystals were dried and distilled in vacuum; b.p. 130-132° at 4 mm. A light-yellow liquid was obtained which quickly crystallized. The yield was nearly quantitative. Recrystallization from aqueous alcohol gave lustrous scales with m.p. 64-65°.

0.2020 g sub.: 14.8 ml N_2 (27°, 768 mm). Found %: N 8.19. $C_{12}H_{15}N$. Calculated %: N 8.09.

The picrate formed dark-red needles with m.p. 143-145° (from aqueous ethanol).

A mixed test of the indoles obtained by the two methods did not give a m.p. depression. A mixed sample of the picrates also melted without depression.

Ethyl α-hydroxy-β-(o-toluidino)-isocaproate

19.5 g ethyl β-methyl-β-ethylglycidate and 22 g (excess) freshly distilled o-toluidine were heated under a reflux condenser closed with a Tishchenko flask containing sulfuric acid. Heating was effected on a bath of Wood's alloy to the b.p. of the reaction mixture (approx. 205°). Heating was continued for 22 hours with interruptions. The anticipated reaction product was distilled at 143-145° (2 mm) in the form of a viscous, light-yellow liquid. Yield 19 g (58 %).

d_4^{20} 1.0760; n_D^{20} 1.5280; MR_D 75.90; Calculated 74.64; EM_D 1.26.

0.1556 g sub.: 7.2 ml N_2 (18°, 764.5 mm): 0.1595 g sub.: 7.8 ml N_2 (21°, 745.4 mm). Found %: N 5.37, 5.44. $C_{15}H_{23}O_3N$. Calculated %: N 5.28.

Synthesis of 2,7-dimethyl-3-ethylindole

13 g ethyl α-hydroxy-β-(o-toluidino)-isocaproate was mixed with 35 ml conc. sulfuric acid. The mixture was heated over a bare flame. At 103° (thermometer in the reaction mixture) bubbles of carbon monoxide started to come off and the process was especially intensive at 110-115°. Carbon monoxide continued to come off for 40-45 minutes and the solution acquired a cherry red color.

After gas had ceased to come off, the mixture was poured into iced water. The reaction product was extracted with ether and then vacuum-distilled. B.p. 123-126° (3 mm). Yield 5 g (59 %).

d_4^{20} 1.0188; n_D^{20} 1.5848; MR_D 56.98; Calculated 54.94; EM_D 2.04. 0.2121 g sub.: 14.8 ml N_2 (15°, 762.2 mm). 0.0998 g sub.: 7.0 ml N_2 (16°, 762 mm). Found %: N 8.18, 8.23. $C_{12}H_{15}N$. Calculated %: N 8.09.

SUMMARY

1. The reaction of ethyl β-methyl-β-ethylglycidate with o- and p-toluidine was investigated. The opening of the oxide ring of the acid was shown to take place from the side of the tertiary β-carbon atom. The previously undescribed ethyl α-hydroxy-β-(p-toluidino)-isocaproate and ethyl α-hydroxy-β-(o-toluidino)-isocaproate were synthesized.

2. Transition was effected from ethyl α-hydroxy-β-(p-toluidino)-isocaproate to 2,5-dimethyl-3-ethylindole, and from ethyl α-hydroxy-β-(o-toluidino)-isocaproate to 2,7-dimethyl-3-ethylindole. Neither of these homologs of indole has been described in the literature.

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HYDROGENATION WITH COLLOIDAL PALLADIUM IN PRESENCE OF INHIBITORS

IV. HYDROGENATION OF METHYL-PHENYL-ETHYNYL CARBINOL

Kh. V. Balyan

In previous communications [1,2] we described the results of our investigations of the hydrogenation with colloidal Pd of acetylenic alcohols, γ-glycol and olefinic alcohols, as well as of the methyl ether of dimethyl-ethynyl carbinol and dimethyl-vinyl carbinol in presence of some organic additives. Some of the latter had a retarding effect upon the course of hydrogenation; others were accelerators. The degree of inhibition in the first and second stage of hydrogenation often differed, thus pointing to a selectivity of the process.

It appeared of interest to follow the course of hydrogenation in presence of inhibitors of analogous compounds with an aromatic radical. For this purpose we selected methyl-phenyl-ethynyl carbinol, the hydrogenation of which, generally speaking, has not been investigated.

The hydrogenation procedure did not differ from that described in previous communications. The hydrogenation products were qualitatively and quantitatively analyzed for compounds with a double and a triple bond.

The olefinic bond was qualitatively determined with the help of bromine water, and the acetylenic bond with an ammoniacal solution of silver oxide or cuprous chloride. Furthermore, for determination of the acetylenic bond we made use of a new test with metallic sodium.

Not devoid of interest was the observation of the differing behavior of methyl-phenyl-ethynyl carbinol and its aliphatic analogs – dimethyl-ethynyl carbinol and methyl-ethyl-ethynyl carbinol toward ammoniacal silver oxide and cuprous chloride. The first alcohol gives a white precipitate of the silver derivative both in aqueous solution and in a solution in methanol or ethanol. The aliphatic analogs, however, do not give corresponding precipitates in methanol or ethanol.

Dimethyl-ethynyl carbinol and methyl-ethyl-ethynyl carbinol do not give characteristic precipitates of copper derivatives in aqueous solutions with an ammoniacal solution of cuprous chloride. At low concentrations of these alcohols, precipitates are not formed even in alcoholic solutions. Methyl-phenyl-ethynyl carbinol, however, gives a characteristic white or yellowish precipitate (depending on the concentration of the alcoholic solutions) not only in aqueous [3] but also in alcoholic solutions.

The metallic sodium test for the triple bond is based on the observation of Zalkind and Bukhovets [4] that heating of γ-acetylenic glycols in alcoholic solution with metallic sodium results in cleavage of the glycol with separation of free acetylene. The latter may be detected with ammoniacal cuprous chloride. We have successfully applied this reaction to acetylenic alcohols, which proved to be extremely sensitive to it. It enabled, for example, 6-10 mg methyl-phenyl-ethynyl carbinol to be detected in solution in 3-4 ml methanol.*

Olefinic compounds were qualitatively determined by the bromate-bromide method [5] and acetylenic compounds with the help of silver nitrate. By this method the original methyl-phenyl-ethynyl carbinol was found to be 99.21% pure.

Methyl-phenyl-ethynyl carbinol was first hydrogenated with an equimolar amount of hydrogen in the absence of inhibitor.

Qualitative and quantitative analysis of the hydrogenation products revealed complete or nearly complete absence of triple-bond compounds. Analysis for double bonds showed that 95.40% methyl-phenyl-vinyl carbinol was present. It can, therefore, be concluded that methyl-phenyl-ethynyl carbinol is strictly selectively hydrogenated in presence of colloidal Pd, i.e. the first two hydrogen atoms add on exclusively at

* This reaction was also found to be applicable to acetylenic-olefinic alcohols of the type of $R_2C(OH)-C\equiv C-CH=CH_2$, where R is methyl or ethyl. When heated with sodium, these alcohols split into the corresponding ketones and vinylacetylene which can be qualitatively detected by the same cuprous chloride and quantitatively determined with an alkaline solution of mercuric iodide in potassium iodide.

the triple bond. It thus behaves like monosubstituted tertiary acetylenic alcohols of the aliphatic series in presence of palladium precipitated on calcium carbonate [6]. On the other hand, the behavior of methyl-phenyl-ethynyl carbinol differs markedly in this respect from that of dimethyl-phenyl-ethynyl carbinol and diphenyl-phenyl-ethynyl carbinol, which (according to Zalkind) are not selectively hydrogenated in these conditions [7].

Parallel experiments were run on hydrogenation of methyl-phenyl-ethynyl carbinol with the same catalyst but in the presence of some inhibitors previously used by us (Table 1).

TABLE 1

No.	Name of inhibitor	Duration of addition of 2H (in min.)	Inhibition during first half of hydrogenation	Content (in %)	
				of methyl-phenyl-ethynyl carbinol	of methyl-phenyl-vinyl carbinol
1	Without inhibitor	5.5; 3.5 *	-	0.76	95.40
2	Without inhibitor**	21 **	-	0	0
3	p-Thiocyanochlorobenzene**	20-30; 130**	4-6 times and 6-7 times in the second half	0	0
4	p-Thiocyanoaniline	9	1 and a half times	3.75	91.83
5	Phenyl mustard oil	18	3 times	0	94.33
6	Chlorobenzene	9	1 and a half times	0	92.64
7	Thiocyano-1-naphthol***	7	2 times	2.74	93.72
8	p-Thiocyanochlorobenzene	30	5 times	4.05	94.29

The influence of inhibitors is shown in Table 1 and Figures 1,2 and 3. The greatest retardation (4-6 times) is caused by p-thiocyanochlorobenzene. A hydrogenation experiment with 0.4 mg p-thiocyanochlorobenzene (0.054%) on the weight of methyl-phenyl-ethynyl carbinol) showed that this amount of inhibitor completely poisons the catalyst, and after 40 minutes not a single milliliter of hydrogen had combined. With a twofold reduction in the amount of this inhibitor (0.2 mg, 0.027%) on the weight of alcohol), hydrogenation took place but very slowly (retardation by a factor of approx. 6 both in the first and in the second stage of hydrogenation).

Results of quantitative analysis of the products of hydrogenation are set forth in Table 1 which shows that the action of chlorobenzene and phenyl mustard oil hardly modifies the composition of the hydrogenation products obtained in the absence of inhibitor. The remaining inhibitors only slightly worsen the selective character of the hydrogenation, leaving from 2.74 to 4.05% of the methyl-phenyl-ethynyl carbinol unreacted. On addition of 2 moles hydrogen to 1 mole acetylenic alcohol, alcohols with a triple or double bond were not detected in the products of hydrogenation.

The product of partial hydrogenation of methyl-phenyl-ethynyl carbinol (methyl-phenyl-vinyl carbinol) was obtained for the first time by Lebedeva and Shlyakova [5]. Methyl-phenyl-vinyl carbinol prepared by us was a perfectly colorless oil free from odor; a triple bond was not detected; the bromate-bromide method indicated a 93.04% content of double-bond compound. The product was obtained in 86% yield. Consequently the hydrogenation of methyl-phenyl-ethynyl carbinol is an extremely convenient method for the preparation of methyl-phenyl-vinyl carbinol.

EXPERIMENTAL****

Methyl-phenyl-ethynyl carbinol was prepared by Zalkind's method [3]; m.p. 50-50.5°.

0.0254 g methyl-phenyl-ethynyl carbinol, 5 ml methanol, 100 ml 2% $AgNO_3$; 1.72 ml KOH (T 0.005630). Indicator was methyl red. Found methyl-phenyl-ethynyl carbinol 0.0252 g, i.e. 99.21% content of pure substance.

Results of quantitative anaylsis of the hydrogenation products are set forth in Table 2.

* First value with 2 mg Pd and the second with 3 mg Pd.

** Hydrogenation took 4H per mole alcohol.

*** Hydrogenated with 3 mg Pd.

**** Quantitative analyses were carried out by L.L. Cherenkova.

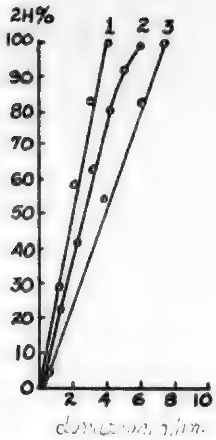

Fig. 1. Hydrogenation of methyl-phenyl-ethynyl carbinol with colloidal palladium

1) with 3 mg catalyst;
2) with 2 mg catalyst;
3) with 2 mg catalyst and 0.2 mg thiocyano 1-naphthol

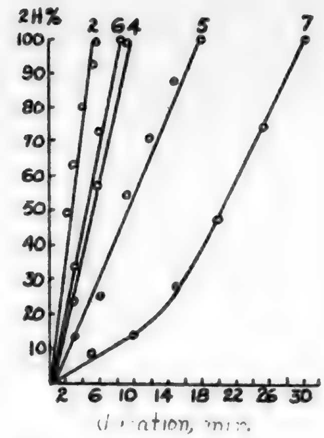

Fig. 2. Hydrogenation of methyl-phenyl-ethynyl carbinol with 2 mg colloidal Pd in presence of inhibitors (see Table 3)

2) with inhibitors; 4) with 0.2 mg p-thiocyanoaniline; 5) with 0.2 mg phenyl mustard oil; 6) with 0.2 mg chlorobenzene; 7) with 0.2 mg p-thiocyano-chlorobenzene.

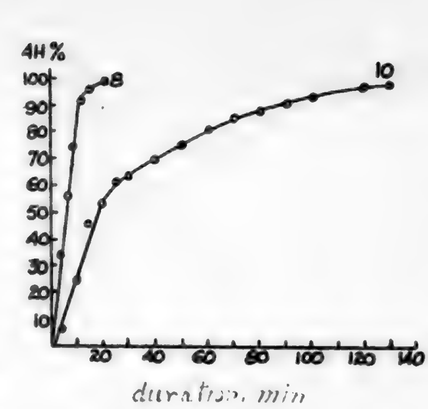

Fig. 3. Hydrogenation of methyl-phenyl-ethynyl carbinol with 2 mg colloidal palladium (see Table 3).

8) without inhibitor;
10) with 0.2 mg p-thiocyanochloro-benzene.

TABLE 2

Analysis of Products of Hydrogenation of Methyl-phenyl-ethynyl Carbinol

(Hydrogenation was effected with 2 H per Mole of Acetylenic Alcohol)

No.	Name of inhibitor	Wt. of methyl-phenyl-ethynyl carbinol (in g)	Consumption of alkali as 0.1 N solution (in ml)	Total content of triple-bond compound (in %)*	Consumption of bromate-bromide as 0.2 N solution (in ml)	Total content of double-bond compound (in %)*
1	Without inhibitor	1.46	0.765	0.76	95.40	95.40
2	Thiocyano-1-naphthol	1.46	2.74	2.74	93.72	93.72
3	Thiocyanoaniline	1.46	3.75	3.75	91.83	91.83
4	Phenyl mustard oil	1.46	0	0	94.33	94.33
5	Chlorobenzene	1.46	0	0	92.64	92.64
6	p-Thiocyanochloro-benzene	1.46	4.05	4.05	94.29	94.29
7	Unhydrogenated methyl-phenyl-ethynyl carbinol	0.0254	1.73	99.21	–	–
8	Without inhibitor**	0.73	0	0	0	0
9	p-Thiocyanochloro-benzene**	0.73	0	0	0	0

* The percentage of triple-bond compound was related to the original weight of methyl-phenyl-ethynyl carbinol; that of double-bond compound was related to the theoretical yield of methyl-phenyl-vinyl carbinol (1.48 g) on the basis of the original weight.

** Hydrogenated with 4 H per mole alcohol.

TABLE 3

0.73 g (0.005 mole) methyl-phenyl-ethynyl carbinol, 40 ml methanol, 2 or 3 ml colloidal Pd (2 or 3 mg Pd), 1 ml alcoholic solution of inhibitor (0.2 mg, or 0.027% of the weight of the acetylenic alcohol); temperature 20°.

No.	Name of inhibitor	Amount of Pd (in mg)	Pressure (mm); calculated for 2 H (in ml)	Duration from start of hydrogenation (in min.)	Amount of hydrogen absorbed from start of reaction (in ml)	(in %)
1	Without inhibitor	3	762; 119	1	35	29.41
				2	70	58.82
				3	100	84.03
				3.5	119	100.0
2	Without inhibitor	2	776;118	1	25	21.18
				2	50	42.37
				3	75	63.56
				4	95	80.51
				5.5	118	100.0
3	Thiocyano-1-naphthol	3	762;119	2	40	33.61
				4	65	54.61
				6	100	84.03
				7	120	100.85
4	p-Thiocyanoaniline	2	758;120	3	28	23.37
				6	70	58.33
				9	120	100.0
5	Phenyl mustard oil	2	758;120	3	15	12.50
				6	30	25.0
				9	65	54.17
				12	85	70.84
				15	105	87.50
				18	120	100.0
6	Chlorobenzene	2	758;120	3	39	32.50
				6	88	73.17
				9	120	100.0
7	p-Thiocyanochlorobenzene	2	763; 120	5	10	8.33
				10	17	14.17
				15	33	27.50
				20	57	47.50
				25	90	75.0
				30	122	101.80
8	Without inhibitor	2	759; 120 and [illegible];4H-240 [illegible]	3	80	33.33*
				6	135	56.25
				9	180	75.0
				12	220	91.67
				15	232	96.67
				18	238	99.15
				21	238	99.15
9	p-Thiocyanochlorobenzene**	2	759; 120 and 4H-240	10	0	
				20	0	0
				30	0	
				40	0	

* Calculated when starting from 240 ml hydrogen.

** 0.4 mg taken.

(Table continued on following page)

TABLE 3 (Continued)

0.73 g (0.005 mole) methyl-phenyl-ethynyl carbinol, 40 ml methanol, 2 or 3 ml colloidal Pd (2 or 3 mg Pd), 1 ml alcoholic solution of inhibitor (0.2 mg, or 0.027%) of the weight of the acetylenic alcohol); temperature 20°.

No.	Name of inhibitor	Amount of Pd (in mg)	Pressure (mm): calculated for 2 H (in ml)	Duration from start of hydrogenation (in min.)	Amount of hydrogen absorbed from start of reaction	
					(in ml)	(in %)
10	p-Thiocyanochlorobenzene	2	759; 120 and 4H - 240	10	60	25.00
				20	130	54.17
				30	153	63.75
				60	195	81.23
				90	220	91.67
				120	236	98.34
				130	239	99.60
11	Without inhibitor*	10	769; 720	2	290	40.24
				4	535	74.30
				6	720	100.0

Hydrogenation of methyl-phenyl-ethynyl carbinol was carried out in the same conditions and with the same apparatus as in the previous communications [1,2].

Results of some experiments on hydrogenation of methyl-phenyl-ethynyl carbinol are set forth in Table 3.

After hydrogenation (expt. 11) the solution was filtered from catalyst and the filter was washed with methanol; the methanol was distilled off and the residual slightly yellow oil was dissolved in ether. The ethereal solution was dried with calcined potassium carbonate, the ether was driven off, and the residual oil distilled in vacuum (0.5 mm). The colorless, transparent oil came over at exactly 62°. A residue of 0.48 g yellow oil in the distillation flask was not investigated.

Amount of product with b.p. 62° (0.5 mm) 3.82 g (86%); d_{20}^{20} 1.0114; d_4^{20} 1.0095 n_D^{20} 1.5338.

According to the literature [5], methyl-phenyl-vinyl carbinol has b.p. 89-90° (5 mm); d_4^{21} 0.9965; n_D^{21} 1.52772; the double-bond content by the bromide-bromate method was 89-90%.

Qualitative anaylsis (with metallic sodium) and quantitative analysis did not reveal the presence of any triple-bond compounds.

Analysis for double bond: 1.1045 g substance, 5 ml methanol, 10 ml water, 3 ml 4 N HCl: 12.5 ml bromate-bromide (T 0.005557); 10 ml 10% KI, 12 ml thiosulfate (T 0.02438, indicator starch solution). Found: methyl-phenyl-vinyl carbinol 0.09723 g (93%).

SUMMARY

1. It was established that methyl-phenyl-ethynyl carbinol, unlike dimethyl-phenyl-ethynyl carbinol and diphenyl-phenyl-ethynyl carbinol, is hydrogenated strictly selectively in presence of colloidal palladium with formation of methyl-phenyl-vinyl carbinol. The method of hydrogenation of methyl-phenyl-ethynyl carbinol for preparation of the vinyl compound has undoubted advantages (speed, purity of product, and high yield of 86%) over other methods.

2. It is shown that some organic compounds thiocyano-α-naphthol, p-thiocyano-aniline, phenyl mustard oil, chlorobenzene, p-thiocyanochlorobenzene - taken in the amount of 9.927% of the weight of methyl-phenyl-ethynyl carbinol, to a greater or lesser degree retard the hydrogenation; p-thiocyanochlorobenzene is particularly effective.

* Methyl-phenyl-ethynyl carbinol was taken in quantity of 4.38 g (0.03 mole); the character of the hydrogenation of this alcohol in quantity of 1.46 g without inhibitor and with inhibitor is analogous to the preceding experiments, and, therefore, is not cited here. The composition of the hydrogenation products is given in Table 2.

Unlike other cases of inhibition, however, this inhibiting action either does not affect the selectivity of hydrogenation or only affects it to a very slight extent.

3. It was established that the test with metallic sodium is an extremely convenient and trustworthy reaction for detecting the presence of acetylenic alcohols.

4. The behavior of methyl-phenyl-ethynyl carbinol toward ammoniacal cuprous chloride differs markedly from that of acetylenic alcohols of the aliphatic series – di methyl-ethynyl carbinol and methyl-ethyl-ethynyl carbinol; the first-mentioned compound gives a characteristic precipitate of the copper derivative; the other two do not.

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* See Consultants Bureau Translation, pp. 793 ff.

** " " " " p. 1285.

IMIDAZOLE DERIVATIVES

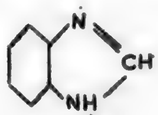
XII. OXIDATION OF 1,2-NAPHTHIMIDAZOLE [1]

B.A. Porai-Koshits, L.N. Kononova and L.S. Efros

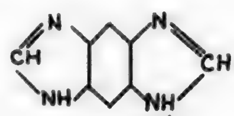
In previous investigations [2,3,4] it was shown that the imidazole ring present in a molecule consisting of condensed rings upsets the bond equivalence of the adjacent rings in the same manner as the benzene ring, for example in naphthalene. In regard to upsetting of bond equivalence, 1,2,4,5-diimidazolo-benzene (II) may thus be compared with anthracene, and benzimidazole (I) with naphthalene.

It was to be expected that this effect of the imidazole ring would also be manifested in the naphthimidazole series. And indeed, not only 1,2,4,5-diimidazolo-benzene (II), but also 2,3-naphthimidazole (III) are reminiscent of anthracene in their properties [5].

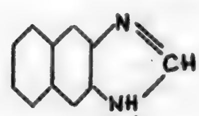
In regard to 1,2-naphthimidazole (IV), whose chemical properties should resemble those of phenanthrene, the literature data are at variance with this hypothesis. Thus, Fischer [6] showed that 1,2-naphthimidazole behaves on oxidation like naphthalene and forms benzimidazole-4,5-dicarboxylic acid (V) - the analog of phthalic acid:



(I)



(II)



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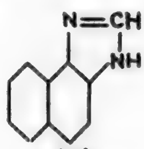

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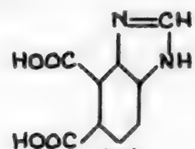


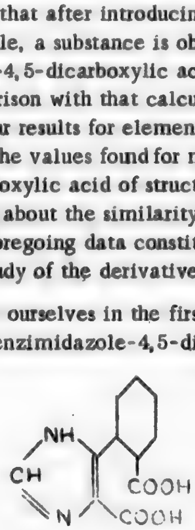
(V)

Fischer appeared to have conclusively demonstrated the structure of this acid by preparing its ester, anhydride, silver salt, anilide, and dyes qualitatively similar to the known phenolphthalein and fluorescein.

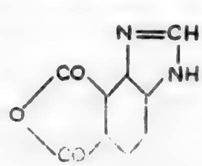
Since according to our theory the most unsaturated bond in 1,2-naphthimidazole must be the 3-4 bond, and oxidation of this product should consequently take place at this bond, we decided to repeat Fischer's experiments and to check the accuracy of his conclusions.

It was found that after introducing more precision into the conditions of carrying out of the oxidation of 1,2-naphthimidazole, a substance is obtained which possesses the same properties as were described by Fischer for benzimidazole-4,5-dicarboxylic acid. Its molecular weight (determined by potentiometric titration), however, was high in comparison with that calculated for (V) (234 instead of 206). Also inconsistent with this formula ($C_9H_6O_4N_2$) were our results for elementary analysis (the latter differed considerably from those given by Fischer). At the same time the values found for molecular weight and elementary composition very closely agreed with those for the dicarboxylic acid of structure (VI) whose formation is consistent with our above-enunicated theoretical considerations about the similarity of 1,2-naphthimidazole to phenanthrene. Since, however, we did not consider that the foregoing data constituted an adequate refutation of Fischer's results, we decided to engage in a more detailed study of the derivatives formed from the compound obtained by oxidation of 1,2-naphthimidazole.

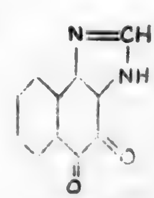
We occupied ourselves in the first instance with the properties of the product which Fischer assumed to be the anhydride of benzimidazole-4,5-dicarboxylic acid (VII):



(VI)



(VII)



(VIII)

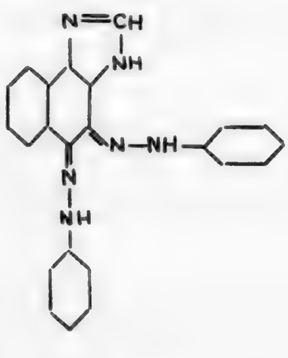
This substance with m.p. 225°, formed by sublimation of the dicarboxylic acid obtained by oxidation of 1,2-naphthimidazole, contained much less nitrogen than was required by formula (VII). The most significant fact, however, was that it was impossible by any means to reconvert it into the original dicarboxylic acid. This substance could be recrystallized from water and it could even be precipitated from alkali solutions with acids in the cold and recovered unchanged. After heating with alkali, however, a new compound crystallized from the acidified solution with a melting point after purification of 203°. After determination of the molecular weight, it was identified as phthalic acid. It was also established that when heated with aqueous alkalies, this "anhydride" evolves ammonia which can be quantitatively collected; the percentage of nitrogen found by this method in the "anhydride" agrees exactly with that found by elementary analysis. We, therefore, arrived at the conclusion that Fischer's "benzimidazole-4,5-dicarboxylic anhydride" is nothing else than phthalimide. This conclusion was confirmed by the identity between the product of sublimation of the dicarboxylic acid obtained by oxidation of 1,2-naphthimidazole and commercial, chemically pure phthalimide.

It is impossible to visualize the formation of phthalimide from benzimidazole-4,5-dicarboxylic acid. Formation of phthalimide confirms the hypothesis that the product of oxidation of 1,2-naphthimidazole has the structure of o-carboxy-phenyl-imidazole-carboxylic acid (VI). Decomposition of the latter during sublimation results in formation also of other products among which could be detected hydrocyanic acid and carbon dioxide.

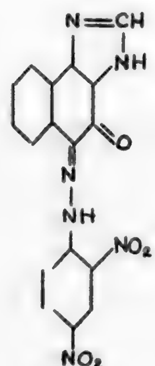
For final confirmation of the accuracy of our proposed scheme for the oxidation of 1,2-naphthimidazole and of the formula of the dicarboxylic acid, it was necessary also to isolate the intermediate product of this reaction – the quinone (VIII) which was not detected by Fischer.

After a number of experiments we succeeded in isolating and characterizing this substance. It forms orange-red crystals, soluble in glacial acetic acid, sulfuric acid and aqueous alkalies with a characteristic violet-red color. This compound gives a hydrazone and dihydrazone of the type of (IX,X), while with o-phenylenediamine and 1,2-naphthalenediamine it forms characteristic azines (XI,XII) - analogs of phenanthrazines.

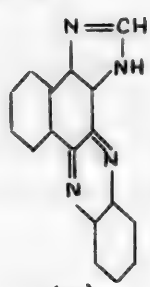
We purified and analyzed all these derivatives. Further oxidation of the quinone gave the already described dicarboxylic acid (VI).



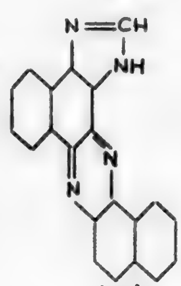
(IX)



(X)



(XI)



(XII)

Consideration must also be given to the analogs of phenolphthalein and fluorescein mentioned by Fischer. Since o-carboxy-phenyl-imidazolecarboxylic acid was unstable, it might be suggested that these dyes are obtained from the products of their breakdown – phthalic acid – and are not analogs of phenolphthalein and fluorescein, as Fischer had thought, but these dyes themselves. Purification of the dyes obtained by interaction of the dicarboxylic acid (VI) with phenol in the first case and with resorcinol in the second case, and the identity

of their absorption spectra with those of the commercial, chemically pure phenolphthalein and fluorescein respectively, confirmed this supposition.

EXPERIMENTAL

Preparation of 1,2-Naphthimidazole.

1,2-Naphthalenediamine was prepared by the known method [7].

Apart from the published methods of preparation [6,8], 1,2-naphthimidazole was synthesized mainly by our proposed method: 25.6 g 1,2-naphthalenediamine sulfate, 10 ml formic acid and 100 ml 10% hydrochloric acid were placed in a round-bottomed flask with a reflux condenser and boiled for 4 hours. After neutralization of the excess acid (violet stain on Congo paper) with aqueous ammonia, the solution was boiled with animal charcoal and filtered hot. The free base 1,2-naphthimidazole was separated from the cooled solution by addition of aqueous ammonia. The base was recrystallized from water or aqueous ethanol and dried at 90-100°; m.p. 174°; yield 14.95 g (89%).

Oxidation of 1,2-Naphthimidazole

1,2-Naphthimidazole was oxidized in a medium of glacial acetic acid with chromic oxide [6]. After recrystallization from water the oxidation product forms white, lustrous crystals melting at 251° and decomposing at 270°.

1,2-Naphthimidazole was also oxidized in sulfuric acid with sodium dichromate, and in this case the product of oxidation was purer and obtained in better yield.

16.8 g 1,2-naphthimidazole was dissolved in 150 ml sulfuric acid diluted with water in the ratio of 1:3. To this solution was gradually added a solution of chromic acid mixture (39.2 g $K_2Cr_2O_7$ in 200 ml 1:3 sulfuric acid) with constant stirring. Oxidation proceeded for 1.5 to 2 hours, after which the green solution was poured into three times the quantity of cold water; fine greenish-yellow crystals came down almost at once. These were filtered after cooling of the solution and washed with iced water until the green color of the wash water had disappeared. The acid was soluble in ethanol, glacial acetic acid and hot water, sparingly soluble in ether and ligroine. Purification was effected by reprecipitation with hydrochloric acid from alkaline solution and by recrystallization from water containing animal charcoal; m.p. 251°; yield 6.9 g (approx. 30%).

0.0986 g sub.: 0.2062 g CO_2; 0.0323 g H_2O. 0.1798 g sub.: 0.3741 g CO_2; 0.0542 g H_2O. 0.1069 g sub.: 11.7 ml N_2 (20°, 735.5 mm). 0.1130 g sub.: 12.3 ml N_2 (19°, 743 mm). Found %: C 57.07, 56.78; H 3.66, 3.37; N 12.23, 12.33. $C_9H_6O_4N_2$. Calculated %: C 52.43; H 2.94; N 13.59. $C_{11}H_8O_4N_2$. Calculated %: C 56.90; H 3.47; N 12.07.

Potentiometric titration of 0.1010 g substance: 8.7 ml 0.1 N NaOH. Found: M 234. $C_{11}H_8O_4N_2$. Calculated: M 232. $C_9H_6O_4N_2$. Calculated M 206.

The analytical results confirm the formula of the dicarboxylic acid (VI) which we advanced on the basis of the considerations set forth in the theoretical part.

Analysis of the silver salt:

1.0116 g sub.: 0.4875 g Ag. 0.3870 g sub.: 0.1877 g Ag. Found %: Ag 48.20, 48.50. $C_9H_4O_4N_2Ag_2$. Calculated %: Ag 51.38. $C_{11}H_6O_4N_2Ag_2$. Calculated %: Ag 48.43.

Dimethyl Ester of the Acid

1 g dicarboxylic acid was boiled for an hour in a solution of methanol (40 ml) with two parts KOH (0.4 g). After cooling, the solution was transferred to a tube to which was added 2 moles methyl iodide (1.42 g); the tube was sealed and heated for 3-4 hours in a gas furnace at 99-100°. After cooling and opening of the tube, the contents were transferred to a porcelain beaker and evaporated to dryness on a water bath. The residue was repeatedly and thoroughly washed with cold water, dried and twice recrystallized from ethanol; m.p. 130°. Yield 7.9 g (71%).

0.1093 g sub.: 0.2383 g CO_2; 0.0439 g H_2O. 0.1417 g sub.: 0.3093 g CO_2; 0.0596 g H_2O. 0.1055 g sub.: 10.1 ml N_2 (20°, 742 mm). 0.1242 g sub.: 12.2 ml N_2 (21°, 744 mm). Found %: C 59.5, 59.57; H 4.50, 4.71; N 10.90, 11.14. $C_{11}H_{10}O_4N_2$. Calculated %: C 56.40; H 4.23; N 12.00. $C_{13}H_{12}O_4N_2$. Calculated %: C 60.00; H 4.65; N 10.76.

Sublimation of the Dicarboxylic Acid

1) The recrystallized and dried substance was placed in a porcelain beaker, covered with an inverted funnel glass and slowly heated on a sand bath. The sublimed material collected on the sides of the funnel in the form of long, very faint-yellow needles with m.p. 225°.

2) Sublimation was effected in vacuum in a refractory flask with a broad tube, heated with an oil bath which enabled regulation of the temperature and avoided overheating of the substance.

0.1514 g sub.: 0.3612 g CO_2; 0.0471 g H_2O. 0.1101 g sub.: 0.2627 g CO_2; 0.0364 g H_2O. 0.1608 g sub.: 13.8 ml N_2 (21°, 740 mm). 0.1426 g sub.: 10.87 ml N_2 (22°, 738 mm). Found %: C 65.10, 65.08; H 3.40, 3.70; N 9.70, 9.66. $C_9H_4O_3N_2$. Calculated %: C 57.40; H 2.20; N 14.97. $C_8H_5O_2N$. Calculated %: C 65.30; H 3.40; N 9.51.

The product of sublimation crystallizes nicely from water and does not revert to the original acid during the process. After two recrystallizations from water it has m.p. 231° and mixed test with the unpurified substance gives m.p. 229°. The substance has good solubility in aqueous alkali and ammonia and remains unchanged when precipitated from an alkaline solution with acids in the cold. Liberation of ammonia was qualitatively observed when the product of sublimation was boiled in aqueous alkali.

A weighed sample of the product of sublimation was placed in a round-bottomed flask and dissolved in 40 ml 15% NaOH solution. The flask was provided with a trap for alkali spray, connected to a sloping water condenser and a receiver; into the flask, below the layer of alkali solution, was inserted a tube for introduction of steam. A standard 0.1N hydrochloric acid solution was placed in the receiver for trapping the ammonia which came off. Distillation was stopped when a drop of the distillate did not turn litmus paper blue. The contents of the receiver were titrated with 0.1 N NaOH solution in presence of methyl orange.

The results of the experiments are set forth in the Table.

Amount of 0.1 N HCl for taking-up of Ammonia = 40 ml

Weight of substance (in g)	Amount of NaOH used in titration (in ml)	N (in %)
0.3076	22.00	9.41
0.2692	24.15	9.65
0.3526	18.31	9.63
0.2962	20.10	9.50

The contents of the distillation flasks were combined, cooled and acidified with dilute hydrochloric acid until acid to Congo paper. Fine white crystals came down which after drying had m.p. 198°. The substance is readily soluble in water and ethanol, poorly in ether and chloroform; it crystallizes nicely from water. After purification, the m.p. is 203°. During the m.p. determination it was observed that if the melted substance was allowed to cool in the capillary and then melted again, it had m.p. 132°, not 203° as originally. The two compounds were identified as phthalic acid and phthalic anhydride. It was thus established that the investigated dicarboxylic acid was transformed into phthalimide during sublimation. After two recrystallizations the product of sublimation was identical in melting point with chemically pure, commercial phthalimide. The elementary analysis gave contents of carbon, hydrogen and nitrogen identical with those for phthalimide.

For the purpose of examination of the other products formed during sublimation of the dicarboxylic acid, the sublimation was effected in a quartz tube heated with a special small gas furnace provided with a thermometer. Sublimation was conducted in a stream of dry air free from carbon dioxide, and was continued for 3 hours. The following products were found as a result of decomposition of the dicarboxylic acid: carbon dioxide (from increase in weight of potash apparatus and from development of turbidity in barytes water) and hydrocyanic acid by qualitative reactions for the CN ion: 1) formation of Prussian blue (in a receiver with 0.1 N hydrochloric acid; 2) the characteristic odor of bitter almonds.

1,2-Imidazole-3,4-naphthoquinone

16.8 g naphthimidazole was dissolved in 150 ml glacial acetic acid or 96-98% acetic acid, heated to the boil, and addition was gradually made with constant stirring of a solution of 6.6 g chromic oxide in 50 ml acetic acid. Duration of oxidation 3-4 hours. The reaction product separated in part on pouring the reaction mass into water and in part after distillation of the acetic acid with steam from this solution. The orange-red crystals had m.p. 318-320° (at 300° the substance darkens and melts unsharply, with decomposition); the product is poorly soluble in cold water, slightly soluble in ethanol, and nearly insoluble in ether and benzene. It dissolves very well in aqueous solutions of alkalies with an intense violet-red color, rather less readily and with a less intense color in aqueous ammonia; on acidification of the alkaline solution it comes down again; it is easily reduced by sodium hydrosulfite in an alkaline medium. The substance was purified by recrystallization from nitrobenzene, washing with ether, and recrystallization from water. Yield 6.6 g (34%).

0.1018 g sub.: 0.2480 g CO_2; 0.0272 g H_2O. 0.0967 g sub.: 0.2350 g CO_2; 0.0275 g H_2O. 0.1235 g sub.: 15.4 ml N_2 (18°, 738 mm). 0.1109 g sub.: 14.01 ml N_2 (20°, 742 mm). Found %: C 66.51, 66.34; H 2.99, 3.18; N 14.2, 14.37. $C_{11}H_6O_2N_2$. Calculated %: C 66.7; H 3.05; N 14.14.

Synthesis of Derivatives of the Quinone

1) 0.5 g quinone was dissolved in the smallest possible amount of ethanol, and to this solution was added excess of phenylhydrazine solution (2 g of the hydrochloride and 3 g sodium acetate in 20 ml water). The solution was refluxed in a flask on a water bath for about a half hour, during which period attractive red crystals of the osazone began to separate in quantity which increased with progressive cooling of the solution. The substance was filtered off and purified by recrystallization from anhydrous ethanol. M.p. above 350°.

0.1073 g sub.: 0.2655 g CO_2; 0.0444 g H_2O. 0.1214 g sub.: 0.3235 g CO_2: 0.0531 g H_2O. 0.0981 g sub.: 19.2 ml N_2 (21°, 738 mm). Found %. C 72.60, 72.71; H 4.63, 4.90; N 22.12. $C_{23}H_{18}N_6$. Calculated %: C 73.04; H 4.76; N 22.20.

2) 2.6 g quinone and 1.53 g p-nitrophenylhydrazine were dissolved in glacial acetic acid and the solution refluxed in a flask for 20-30 minutes. On cooling the hydrazone crystallizes in the form of fairly large red crystals which were filtered and recrystallized from glacial acetic acid. M.p. above 350°.

0.1036 g sub.: 20.4 ml N_2 (20°, 742 mm). 0.0975 g sub.: 19.3 ml N_2 (21°, 740 mm). 0.1106 g sub.: 0.2428 g CO_2; 0.0375 g H_2O. 0.1094 g sub.: 0.2473 g CO_2; 0.0385 g H_2O. Found %. C 59.93, 61.67; H 3.80, 3.94; N 22.42, 22.41. $C_{17}H_{11}O_3N_5$. Calculated %: C 61.30; H 3.76; N 22.10.

3) 2 g dinitrophenylhydrazine was dissolved in 4 ml warm conc. sulfuric acid and diluted with 25 ml anhydrous ethanol. A solution of 2.6 g of the quinone in methanol was added in one portion to this solution, and the mixture was refluxed for a short time in a flask. Red crystals of the hydrazone separated even from the hot solution; after cooling they were filtered, washed with a small quantity of anhydrous ethanol and recrystallized from nitrobenzene. M.p. above 350°.

0.1011 g sub.: 0.1988 g CO_2; 0.0251 g H_2O. 0.1024 g sub.: 20.0 ml N_2 (22°, 742 mm). Found %: C 53.67; H 2.78; N 22.06. $C_{17}H_{10}O_5N_6$. Calculated %: C 54.00; H 2.60; N 22.20.

4) 2.6 g quinone was dissolved in boiling water and into this solution was run a boiling aqueous solution of 1.08 g o-phenylenediamine. Heating was continued for about 3 hours until separation of the yellow precipitate of the azine (XI) had ceased. Yield 2.16 g (78%).

0.1716 g sub.: 0.4720 g CO_2; 0.0558 g H_2O. 0.1207 g sub.: 22.5 ml N_2 (20°, 736 mm) 0.0851 g sub.: 15.9 ml N_2 (21°, 734 mm). Found %. C 75.08; H 3.64; N 21.02, 20.97. $C_{17}H_{10}N_4$. Calculated %: C 75.30; H 3.57; N 20.73.

5) 2.6 g quinone was condensed with 1.58 g 1,2-napththalenediamineas in the preceding case. Yield of azine (XII) 2.3 g (72%). Melting point of both azines above 350°.

0.1142 g sub.: 0.3284 g CO_2; 0.0390 g H_2O. 0.0915 g sub.: 14.47 ml N_2 (22°, 740). Found %: C 78.47; H 3.91; N 17.83. $C_{21}H_{12}N_4$. Calculated %: C 78.75; H 3.75; N 17.50.

Oxidation of the Quinone

5 g quinone was dissolved in 75 ml sulfuric acid (1:3) and to this solution was gradually added 6 g potassium bichromate. Oxidation was continued for 50-60 minutes, after which the reaction mass was poured into water; 6-8 hours later the small amount of substance was filtered off and after recrystallization from water and drying it had m.p. 251° and was identified as 5-phenylimidazole-3,4-dicarboxylic acid. Yield 0.43 g (approx. 8%).

SUMMARY

1. Further consideration of the previously developed concepts of the influence of the imidazole ring on the benzene ring condensed with it points to chemical similarity between 1,2-naphthimidazole and phenanthrene.

2. An experimental study of the oxidation of 1,2-naphthimidazole confirms this conclusion. This study shows that the reaction at first leads to formation of 1,2-naphthimidazole-3,4-quinone, which further oxidizes to phenylimidazole-dicarboxylic acid. The latter was erroneously assumed by Fischer to be 3,4-benzimidazole-dicarboxylic acid.

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REACTION OF NITROSTYRENE WITH SOME COMPOUNDS CONTAINING METHYLENE GROUPS ACTIVATED BY CARBONYL AND CARBOXYL GROUPS

V.V. Perekalin and A.S. Sopova

We have studied the interaction of β-nitrostyrene with substances containing labile hydrogen atoms in the methylene and methyl groups.

The hydrogen atoms were activated by electronophilic groups (carboxyl, carbonyl, cyano, and also by the nitrogen atoms of heterocycles) located in the alpha-position to, or conjugated with, methylene and methyl groups.

Literature data about the reaction of nitroolefins with compounds containing active methyl and methylene groups are scanty [1-3].

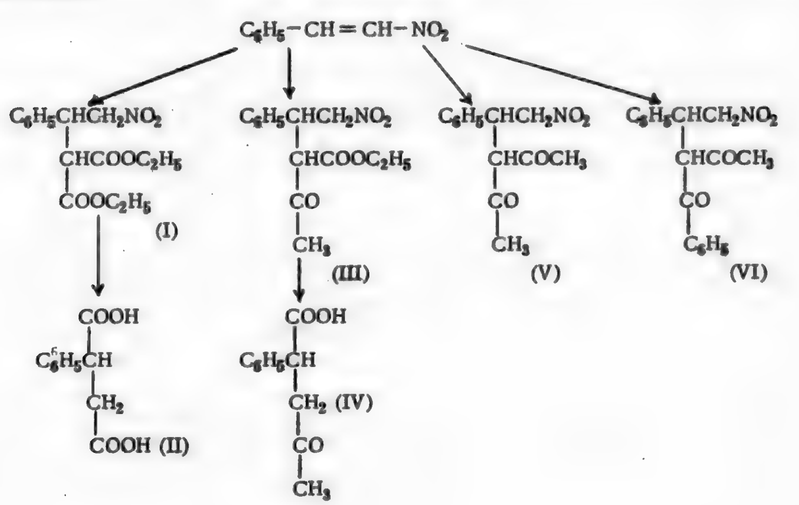
In the first instance we investigated the reaction of nitrostyrene with compounds in which the methylene group was activated by carboxyl and carbonyl groups, (ethyl malonate and ethyl acetoacetate, acetylacetone and benzoylacetone). Reaction was conducted in a medium of methanol or benzene in the cold and with heating in presence of basic catalysts - sodium and potassium methoxides and triethylamine.

The reaction of nitrostyrene with ethyl malonate led to formation of a condensation product - the ethyl ester of 1-nitro-2-phenyl-3-carbethyl-butyric acid (I)*. Its structure was confirmed by hydrolysis in an acid medium which gave, in accordance with the literature data, phenylsuccinic acid (II).

Ethyl acetoacetate entered into reaction with nitrostyrene and formed ethyl 1-nitro-2-phenyl-3-acetyl-butyrate (III); the end product of hydrolysis in an acid medium was 2-phenyl-4-ketovaleric acid (IV).

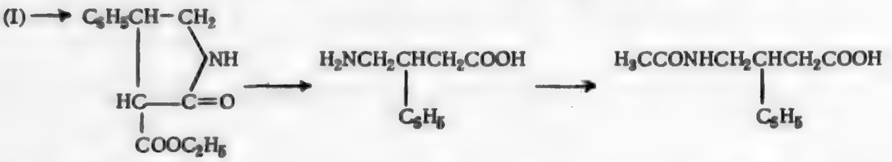
Reaction of nitrostyrene with acetylacetone and benzoylacetone led to synthesis of two condensation products: 1-nitro-2-phenyl-3-acetyl-4-pentanone (V) and 1-nitro-2-phenyl-3-benzoyl-4-pentanone (VI).

Nitrostyrene did not react with methylethyl ketone in which the methylene group was activated only by one carbonyl group.



* In the nomenclature common outside Russia this acid might be named: α-carb-ethyl-β-phenyl-γ-nitrobutyric acid. Similar consideration apply to other compounds in this paper. Publisher.

Only a few methods of synthesis of γ-aminobutyric acid are known [4]; reactions leading to formation of its derivatives are even less developed [5]; special attention was, therefore, given to investigation of the transformations of the product of condensation of nitrostyrene with ethyl malonate with the aim of synthesizing derivatives of γ-amino acids. Reduction of (I) with hydrogen in presence of nickel catalyst led to a nearly quantitative yield of 3-phenyl-4-carbethoxy-5-pyrrolidone (VII), prolonged heating of which with 20% hydrochloric acid transformed it into 1-amino-2-phenyl-butyric acid (VIII) (75.6%). This amino acid, in contrast to the lactam (VII), readily and quantitatively gives the reaction for a primary amino group with nitrous acid, and when heated with acetic anhydride it formed 1-acetylamino-2-phenyl-butyric acid (IX) (yield 76.4%).



(VII) (VIII) (IX)

EXPERIMENTAL

1. Preparation of Ethyl 1-Nitro-2-phenyl-3-carbethyl-butyrate [1]

To a solution of sodium ethyl malonate, prepared by adding 1 g sodium to a mixture of 7.2 g (0.045 mole) ethyl malonate in 50 ml dry methanol, was added at 10-15° a solution of 5.2 g (0.035 mole) β-nitrostyrene in 50 ml dry methanol; the mixture was heated in the absence of moisture for 2 hours at 50-55°. After cooling, the red solution was neutralized with 100% acetic acid and then saturated at 0-5° with dry hydrogen chloride until acidic; on pouring the light-yellow solution into a mixture of salt and sodium carbonate, a resin came down which gradually solidified when rubbed. After 12 hours the precipitate was filtered and after washing with water it was crystallized from methanol. The ester (I) formed white, star-shaped crystals, m.p. 64°, easily soluble in methanol, ethanol, acetone, and benzene. Yield 5.5 g (51.4%).

0.1023 g sub.: 6.8 ml N_2 (18°, 770 mm). 0.1160 g sub.: 4.7 ml N_2 (14°, 750 mm). 0.2200 g sub.: 11.96 g benzene; Δt 0.31°. Found %: N 4.72, 4.73; M 303. $C_{15}H_{19}O_6N$. Calculated %: N 4.53; M 309.2.

2. Transformation of Ethyl 1-Nitro-2-phenyl-3-carbethyl-butyrate into Phenylsuccinic Acid

A weighed amount of 1 g (I) in 100 ml 18% hydrochloric acid was boiled for 12 hours; the whole of the solid gradually went into solution. The crystals separating after cooling of the solution had m.p. 167°; the literature [6] gives m.p. 167°.

3. Preparation of Ethyl 1-Nitro-2-phenyl-3-acetylbutyrate

Into a mixture consisting of a solution of 2.08 g (0.014 mole) nitrostyrene in 20 ml anhydrous benzene and 2.6 g (0.020 mole) ethylacetoacetate was introduced 3 drops triethylamine. Evaporation of the solution 10 hours later caused separation of white crystals of ethyl 1-nitro-2-phenyl-3-acetylbutyrate with m.p. 76° (from ethanol). Yield 3.8 g (98%).

0.1134 g sub.: 0.2512 g CO_2; 0.0615 g H_2O. 0.1185 g sub.: 0.2622 g CO_2; 0.0660 g H_2O. 0.1253 g sub.: 5.3 ml N_2 (14°, 776 mm). 0.1521 g sub.: 6.6 ml N_2 (17°, 761 mm). 0.1665 g sub.; 14.19 g benzene Δt 0.22°. 0.1094 g sub.: 14.81 g benzene Δt 0.13°. Found %: C 60.45, 60.38; H 6.06, 6.23; N 5.09, 5.07; M 272, 275. $C_{14}H_{17}O_5N$. Calculated %: C 60.18; H 6.13; N 5.01; M 279.

4. Preparation of 2-Phenyl-4-ketovaleric Acid

1.4 g ethyl 1-nitro-2-phenyl-3-acetylbutyrate in 140 ml 18% hydrochloric acid was boiled for 12 hours; gradually the whole of the resinous precipitate dissolved. Filtration of the red solution followed by evaporation to 1/10 of its original volume led to gradual separation of a light-yellow substance, m.p. 127° (from ethanol); the literature reports m.p. 127° [7].

5. Preparation of 1-Nitro-2-phenyl-3-acetyl-4-pentanone

To a mixture consisting of a solution of 1.5 g (0.01 mole) nitrostyrene in 15 ml anhydrous benzene and 1.2 g (0.012 mole) acetylacetone was added 3 drops triethylamine. After 10 hours the solution was evaporated and yielded acicular crystals of 1-nitro-2-phenyl-3-acetyl-4-pentanone with m.p. 114° (from ethanol). Yield 2 g (77.7%).

0.1139 g sub.: 0.2606 g CO_2; 0.0685 g H_2O. 0.1294 g sub.: 6.6 ml N_2 (17°, 752 mm). 0.1136 g sub.: 5.7 ml N_2 (16°, 765 mm). Found %: C 62.43; H 6.72; N 5.89, 5.92. 0.1011 g sub.; 14.24 g benzene: Δt 0.15°. 0.1981 g sub.; 14.24 g benzene: Δt 0.28°; M 241, 253. $C_{13}H_{15}O_4N$. Calculated %: C 62.61; H 6.69; N 5.62; M 249.

6. Preparation of 1-Nitro-2-phenyl-3-benzoyl-4-pentanone

To a mixture prepared by mixing a solution of 1.5 g (0.01 mole) nitrostyrene in 15 ml anhydrous benzene with 1.62 g (0.01 mole) benzoylacetone in 10 ml anhydrous benzene was added 3 drops triethylamine. Evaporation of the solution after 10 hours gave a resinous mass which after trituration with ethanol changed into white crystals.

1-Nitro-2-phenyl-3-benzoyl-4-pentanone had m.p. 131° (from ethanol). Yield 2.7 g (86%).

0.1132 g sub.: 0.2875 g CO_2; 0.0580 g H_2O. 0.1039 g sub.: 0.2638 g CO_2; 0.0528 g H_2O. 0.1080 g sub.: 4.3 ml N_2 (23°, 769 mm). 0.1153 g sub.: 4.6 ml N_2 (20°, 759 mm). 0.1037 g sub.; 14.10 g benzene Δt 0.13°. 0.2194 g substance: 14.10 g benzene: Δt 0.26°. Found %: H 5.73, 5.68; N 4.60, 4.60; M 238, 303. $C_{18}H_{17}O_4N$. Calculated %: C 69.42; H 5.57; N 4.50; M 311.

7. Preparation of 3-Phenyl-4-carbethoxy-5-pyrrolidone

5 g specially prepared nickel catalyst [8] and 70 ml methanol were saturated with hydrogen in the course of 2 hours with energetic stirring until the gas ceased to be absorbed at room temperature. Addition was then made in a hydrogen stream of 5 g ethyl 1-nitro-2-phenyl-3-carbethyl-butyrate in 10 ml methanol. Hydrogenation was carried out at 30-40° with vigorous shaking; in 5 hours 1000 ml hydrogen was absorbed (the calculated amount was 1050 ml). The catalyst was then removed by filtration and the alcoholic filtrate evaporated to 0.1 of its original volume. After 12-14 hours 3-phenyl-4-carbethoxy-5-pyrrolidone separated (white crystals) with m.p. 132° (from methanol), easily soluble in methanol and ethanol, less readily in water; stable to heating in water (no change when heated for 2 hours at 180-190°). A positive reaction for a primary amino group (nitrogen liberation) occurs when an aqueous solution of the substance and sodium nitrite is treated with a twofold excess of hydrochloric acid on a boiling water bath (the reaction does not go in the cold). Yield 3.53 g (97%).

0.1243 g sub.: 0.3044 g CO_2; 0.0720 g H_2O. 0.1149 g sub.: 0.2813 g CO_2; 0.0680 g H_2O. 0.1107 g sub.: 6.2 ml N_2 (19°, 742.5 mm). 0.1273 g sub.: 6.7 ml N_2 (18°, 767.5 mm). 0.1553 g sub.: 13.31 g benzene: Δt 0.27°. 0.2784 g substance; 13.31 g benzene: Δt 0.46°. Found %: C 66.82, 66.81; H 6.48, 6.62. N 6.34, 6.18; M 220, 231. $C_{13}H_{15}O_3N$. Calculated %: C 66.91; H 6.48; M 233.

8. Preparation of 1-Amino-2-phenyl-butyric Acid

3 g 3-phenyl-4-carbethoxy-5-pyrrolidone was boiled for 16 hours in 300 ml 18% hydrochloric acid; the whole of the solid gradually dissolved. The product obtained by evaporating the solution on a water bath (m.p. 195°) was dissolved in 10 ml water and neutralized with 10% aqueous sodium carbonate. The solution was twice treated with 25 ml ether and evaporated to 0.1 of the original volume. Dilution with double the amount of ethanol caused separation of the acid as white acicular crystals with m.p. 209° (from aqueous ethanol). The acid is readily soluble in cold water, pH of aqueous solution 6.5; it is insoluble in methanol, ethanol, acetone, chloroform, carbon tetrachloride, benzene and pyridine. Yield 1.74 g (75.6%).

0.1111 g sub 0.2724 g CO_2; 0.0750 g H_2O. 0.1428 g sub.: 0.3521 g CO_2; 0.0966 g H_2O. 0.1091 g sub.: 7.3 ml N_2 (17°, 768.5 mm). 0.1121 g sub.: 7.4 ml N_2 (17°, 770.5 mm). 0.0103 g sub.: 0.1069 g camphor Δt 23°. 0.0101 g substance; 0.1050 g camphor: Δt 22°. Found %: C 66.9, 67.28; H 7.55, 7.51; N 7.90, 7.82; M 167.5, 174.8. $C_{10}H_{13}O_2N$. Calculated %: C 66.99; H 7.31; N 7.82; M 179.

The primary amino group was determined by the usual procedure of acting on a hydrochloric acid solution of the amino acid with aqueous sodium nitrite.

0.1000 g sub.: 6.8 ml N_2 (17°, 761 mm). 0.0900 g sub.: 6.2 ml N_2 (17°, 765.5 mm). Found %: N 7.95, 8.10. $C_{10}H_{13}O_2N$. Calculated %: N 7.82.

9. Preparation of 1-Acetylamino-2-phenyl-butyric Acid

1.5 g 1-amino-2-phenyl-butyric acid and 15 ml acetic anhydride were boiled for 3 hours; after cooling, the solution was filtered and neutralized with 10% aqueous sodium carbonate to bring down a precipitate of 1-acetylamino-2-phenyl-butyric acid in the form of lustrous lozenges with m.p. 65° (from n-hexane). The substance is insoluble in water, soluble in methanol, ethanol, acetone, chloroform, and n-hexane. Yield 1.4 g (76.4%).

0.0916 g sub.: 5.2 ml N_2 (16°, 752 mm). Found %: N 6.59. $C_{12}H_{15}O_3N$. Calculated %: N 6.33.

SUMMARY

1. It is shown that nitrostyrene reacts in presence of basic catalysts with various compounds containing methylene groups activated by carbonyl and carboxyl groups.

2. A new method of synthesis of derivatives of γ-amino acids is proposed.

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* This patent no. and year are as given in the original journal. Publisher.

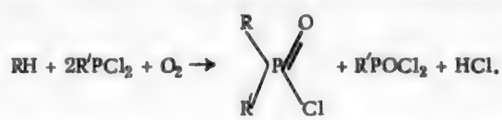
SYNTHESIS OF ORGANOPHOSPHORUS COMPOUNDS FROM HYDROCARBONS AND THEIR DERIVATIVES

IV. FORMATION OF DERIVATIVES OF DIALKYLPHOSPHINIC ACIDS FROM ALKYLDICHLOROPHOSPHINES, HYDROCARBONS AND OXYGEN

L.Z. Soborovsky and Yu. M. Zinovyev

We previously effected reactions of phosphorus trichloride and oxygen with paraffinic, olefinic and acetylenic hydrocarbons and some of their derviatives [1,2,3]. It was considered expedient to investigate the possibility of formation of a phosphorus-carbon linkage in the conditions of the described process when phosphorus trichloride was replaced by certain other compounds containing phosphorus in the trivalent state. As compounds of this type we selected alkyldichlorophosphines, since in their case we should expect formation of derivatives of secondary (including mixed) dialkylphosphinic acids. As we know, the starting dialkylchlorophosphines, as well as the aryldichlorophosphines, have become relatively accessible compounds as a result of recently published researches [4,5].

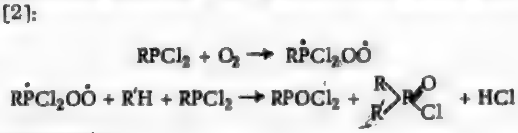
The experimental work confirmed the above suggestion: on passing oxygen through a mixture of methyl- or ethyldichlorophosphine and propane, cyclohexane or allyl chloride, the chlorides of the corresponding secondary phosphinic acids were obtained, i.e. the chlorides of methylpropyl-, methylcyclohexyl-, ethylcyclohexyl- and ethyldichloropropylphosphinic acids. At the same time methyl- or ethyldichlorophosphine were formed as products of direct oxidation, i.e. the acid chlorides of methane- or ethanephosphinic acid:



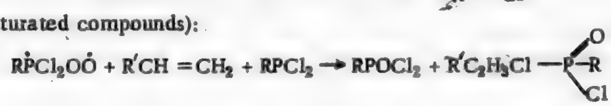
The application in this reaction of compounds so diverse in character as propane, cyclohexane and allyl chloride demonstrates that the reaction of alkyldichlorophosphines with oxygen and aliphatic hydrocarbons can be extended to a great number of diverse compounds of the paraffinic, olefinic and, apparently, acetylenic series.

In the reaction considered, just as in those previously described, the main process is the oxidation of the initial trivalent phosphorus compound. A large proportion of the alkyldichlorophosphines is thereby transformed into alkanephosphinyl chlorides. These chlorides are formed in a yield of 20-25% reckoned on the reacted alkyldichlorophosphine. Thus, for example, on reaction with allyl chloride, 58% of the initial ethyldichlorophosphine was transformed into ethyldichloroxyphosphine and only 14% into ethyldichloropropylphosphinyl chloride.

The mechanism of the reaction in question may be represented by the following scheme, in analogy with that previously described [2]:



or (in the case of unsaturated compounds):



EXPERIMENTAL

Preparation of Methylpropylphosphinyl Chloride (I)

In a reactor, fitted with a gas-leading tube, was placed 114 g methyldichlorophosphine (0.974 mole). The reactor was cooled in a mixture of carbon dioxide and acetone, and 97 g propane (1.975 mole) was

condensed in it. Through the mixture at -60° was passed oxygen. The evolved gases passed through a carbon dioxide trap and then into the fume cupboard. The propane condensing in the trap was returned to the reactor. Passage of oxygen was continued until the reaction mass in the reactor had changed into a crystalline mass. The temperature in the reactor was gradually raised and at the end of the experiment was -5°. For removal of low-boiling reaction products, the mass was heated on a bath to 140°, at first at atmospheric pressure and later at 25 mm. The residue after distillation of the methyldichloroxyphosphine was distilled at 73-85° (3-4 mm). 16.9 g substance came over On redistillation the main mass of substance boiled at 78-81° (4 mm); d_4^{20} 1.1307; n_D^{20} 1.4628.

3.790 mg sub.: 4.620 mg CO_2; 2.920 mg H_2O. 4.440 mg sub.: 5.450 mg CO_2; 2.785 mg H_2O. 0.1547 g sub.: 11.11 ml 0.1 N $AgNO_3$. 0.1118 g substance: 8.06 ml 0.1 N $AgNO_3$. 4.525 mg substance: 69.460 mg $(NH_4)_3PO_4 \cdot 12MoO_3$. 8.690 mg substance: 133.800 mg $(NH_4)_3PO_4 \cdot 12MoO_3$. 0.4408 g substance: 12.55 ml 0.5 N NaOH. Found %: C 33.55, 33.50; H 6.92, 7.01; Cl 25.50, 25.6; P 22.32, 22.39; equiv. 2.025. $C_4H_{10}OClP$. Calculated %: C 34.17; H 7.17; Cl 25.22; P 22.03; equiv. 2.00.

Preparation of Methylcyclohexylphosphinyl Chloride (II)

A stream of oxygen from a cylinder was passed for 5 hours through a mixture of 51 g cyclohexane and 136 g methyldichlorophosphine at 20-25°. The low boiling substances (unreacted cyclohexane and methyldichlorophosphine) were then distilled off from the reaction mixture at atmospheric pressure, and 21 g cyclohexane was collected. After removal of the methyldichlorophosphine (at 20 mm), the residue came over at 110-128° (2 mm). Yield 28.6 g. On redistillation the substance boiled at 101-102° (3 mm), and solidified at 26°; d_4^{20} 1.1611; n_D^{20} 1.4988.

0.2226 g sub.: 12.33 ml 0.1 N $AgNO_3$. 0.2243 g sub.: 12.55 ml 0.1 N $AgNO_3$. 6.370 mg sub.: 74.830 mg $(NH_4)_3PO_4 \cdot 12MoO_3$. 6.500 mg substance: 74.460 mg $(NH_4)_3PO_4 \cdot 12MoO_3$. Found %: Cl 19.65, 19.87; P 16.62, 16.66. $C_7H_{14}OClP$. Calculated %: Cl 19.63; P 17.15.

Properties of Synthesized Substances

No. of compound	Formulas of synthesized compounds	M.p.	B.p. (pressures in mm in brackets)	d_4^{20}	n_D^{20}	MR_D Found	MR_D Calculated	Yield in % of hydrocarbon consumed)
(I)	$\begin{matrix}CH_3\\C_3H_7\end{matrix}>POCl$	-	78-81 (4)	1.1307	1.4628	34.21	33.50	25
(II)	$\begin{matrix}CH_3\\C_6H_{11}\end{matrix}>POCl$	26	101–102 (3)	1.1611	1.4988	45.65	45.14	44
(III)	$\begin{matrix}C_2H_5\\C_6H_{11}\end{matrix}>POCl$	-	118 (3)	1.1372	1.5002	50.35	49.76	68
(IV)	$\begin{matrix}C_2H_5\\C_3H_5Cl_2\end{matrix}>POCl$	-	115–120 (2)	1.3492	1.4980	48.55	47.84	47
(V)	$C_2H_5POCl_2$*	-	45–46 (3)	1.3678	1.4661	29.80	29.49	58 (on amount taken in the reaction)

Preparation of Ethylcyclohexylphosphinyl Chloride (III)

Dry oxygen was passed through a mixture of 84.5 g (0.645 mole) ethyldichlorophosphine and 27.2 g (0.324 mole) cyclohexane until the reaction mass ceased to evolve heat. Then at atmospheric pressure the unreacted cyclohexane (22.2 g) was distilled off, followed in vacuum (20 mm) by the ethyldichlorophosphine and ethyldichloroxyphosphine. The residue was distilled at 110-130° (4 mm). Yield 68% calculated on the cyclohexane consumed. On redistillation the main fraction came over at 118-119° (3 mm).

d_4^{20} 1.1372; n_D^{20} 1.5002.

3.681 mg sub.: 6.600 mg CO_2; 2.720 mg H_2O. 4.352 mg sub.: 7.775 mg CO_2; 3.335 mg H_2O. 0.2101 g sub.: 10.7 ml 0.1 N $AgNO_3$. 0.1978 g sub.: 10.2 ml 0.1 N $AgNO_3$. Found %: C 48.93, 48.58; H 8.26, 8.60; Cl 18.04, 18.29. $C_8H_{16}OClP$. Calculated %: C 49.34; H 8.29; Cl 18.23.

* The compound was first prepared by Michaelis [6] and characterized by Guichard [7]. The latter erroneously attributes to ethyldichlorophosphine d_4^{20} 1.1883.

Preparation of Ethyldichloropropylphosphinyl Chloride (IV)*

Dry oxygen was passed through a mixture of 54.8 g (0.418 mole) ethyldichlorophosphine and 34.6 g (0.452 mole) allyl chloride until heat evolution by the reaction mass had ceased. From the reaction mass was distilled 18.6 g unreacted allyl chloride, 35.8 g ethanephosphinyl chloride, and 16.5 g of a high-boiling product which came over up to 120° (3 mm). Redistillation gave a 115-120° (2 mm) fraction; d_4^{20} 1.3492; n_D^{20} 1.4980. Yield 47% reckoned on the allyl chloride consumed.

3.875 mg sub.: 3.790 mg CO_2; 1.810 mg H_2O. 4.225 mg sub.: 4.200 mg CO_2; 2.165 mg H_2O. 0.1436 g sub.: 6.53 ml 0.1 N $AgNO_3$. 0.0668 g sub.: 3.05 ml 0.1 N $AgNO_3$. Found %: C 26.69, 27.12; H 5.23, 5.73; Cl** 16.13, 16.21. $C_5H_{10}OCl_3P$. Calculated %: C 26.90; H 4.51; Cl** 15.86.

SUMMARY

1. It is shown that a C–P bond is formed on interaction of hydrocarbons of the aliphatic series or their chloro derivatives with oxygen and alkyldichlorophosphines.

2. Chlorides of secondary (mixed) dialkylphosphinic acids were prepared. The reaction was effected between methyl- or ethyldichlorophosphines and propane, cyclohexane or allyl chloride.

3. The chlorides of methylpropyl-, methylcyclohexyl-, ethylcyclohexyl- and ethyldichloropropylphosphinic acids were synthesized.

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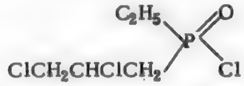
* See Consultants Bureau Translation, p. 391.

* The compound is apparently a mixture of the isomers



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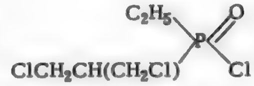

The question of the position of the chlorine atoms in the hydrocarbon radical of the compound prepared is not considered in the present communication.

** Identified as hydrolyzable chlorine.

REACTION OF TRIPHENYLANTIMONY WITH THE SODIUM SALT OF N-BROMOACETAMIDE

L.P. Petrenko

Representatives of organometallic compounds of elements of the fifth group of Mendeleev's periodic system with salts of N-chloroamides which have been studied are organoarsenic and organophosphorus compounds [1,2,3]. A general feature of this reaction is that, depending on the reaction conditions, formation occurs of arsine oxides or of hydroxy derivatives of arsineimines when the reaction takes place in presence of moisture:

$$(C_6H_5)_3As + ArSO_2NNaCl \xrightarrow{HOH} (C_6H_5)_3AsO + ArSO_2NH_2 + NaCl$$

$$(C_6H_5)_3As + ArSO_2NNaCl \xrightarrow{HOH} (C_6H_5)_3As\begin{matrix} OH \\ NHSO_2Ar \end{matrix} + NaCl$$

On carrying out the reaction in the absence of moisture, however, there is a quantitative yield of arsineimines:

$$(C_6H_5)_3As + ArSO_2NNaCl \longrightarrow NaCl + (C_6H_5)_3AsNSO_2Ar.$$

Tertiary phosphines react in exactly the same manner with N-chloroamides. Nothing has been published in the literature about the reactions of organoantimony compounds with salts of N-chloroamides.

Since phosphorus, arsenic and antimony occur in the same group of the periodic system and since organophosphorus and organoantimony compounds react with sodium salts of N-chloroamides when simply brought together both in solvents and without solvents, we inferred that triphenylantimony would also react with sodium salt of N-bromoacetamide with formation of the stibineimine. The experimental work on these lines did not confirm our predictions although the reactions were performed in a variety of conditions (duration, temperature, solvents, and ratios of reactants). Only the addition of a small amount of conc. hydrochloric acid as catalyst gave the opportunity of obtaining the condensation product — triphenylantimonyacetimine:

$$(C_6H_5)_3Sb + CH_3CONNaBr \longrightarrow NaBr + (C_6H_5)_3SbNCOCH_3.$$

The composition of triphenylantimonyacetimine was confirmed both by quantitative analysis for antimony and nitrogen and by formation of derivatives with copper chloride and mercury chloride. Analysis established that one mole of triphenylantimonyacetimine reacts with one mole of copper chloride or mercury chloride.

EXPERIMENTAL

The triphenylantimony required for the investigations was synthesized from antimony trichloride, bromobenzene and magnesium powder in a medium of anhydrous ether [4]. After purification from diphenyl and other impurities by vacuum distillation, it formed white crystals with m.p. 49-50° and b.p. 220° at 12 mm.

The sodium salt of N-bromoacetamide was obtained by reacting acetamide with sodium hypobromide [5] followed by salting-out with acetone at a temperature of -10 to -15°; it formed white, hygroscopic crystals.

Found%: active Br 50.06, 49.55; N 8.52. $C_2H_3ONNaBr$. Calculated %: active Br 49.95; N 8.76.

Reaction of triphenylantimony with sodium salt of N-bromoacetamide. 3.5 g (0.01 mole) triphenylantimony was dissolved in 40 ml anhydrous acetone and to the solution in several portions was added 1.92 g (0.01 mole) sodium salt of N-bromoacetamide. No changes were observed. On adding 2-3 drops of conc. hydrochloric acid to the reaction mass, however, the solution became turbid and the temperature rose from 18 to 27°. The reaction was concluded by heating for another 30 minutes at 50° on a water bath; the precipitate, consisting of sodium bromide and unreacted sodium salt of N-bromoacetamide, was filtered off, and the mother liquor was evaporated in a vacuum at room temperature to a small volume. On cooling to -10°, the residual liquid in the flask crystallized. The crystals were filtered off, washed with anhydrous ether and dried in a desiccator. After recrystallization from anhydrous ether, triphenylantimonyacetimine had m.p. 157-159°. Yield 3.06 g or 74.63% of the theoretical. The white crystalline compound has good solubility in chloroform, acetone and benzene; it is sparingly soluble in

ether and ethanol, insoluble in water. The pH of the aqueous ethanolic solution at the quinhydrone electrode was 6.1.

0.0684 g sub.: 1.53 ml 0.1 N H_2SO_4. 0.0720 g sub.: 3.5 ml 0.1 N $Na_2S_2O_3$. Found %: N 3.12; Sb 29.59. $C_{20}H_{18}ONSb$. Calculated %: N 3.42; Sb 26.69.

Derivatives of triphenylantimonyacetimine with mercury chloride and copper chloride were prepared for confirmation of the structure.

0.35 g triphenylantimonyacetimine was dissolved in 5 ml chloroform, and into the solution was run 5 ml 5% solution of mercuric chloride in ethanol. After 24 hours 0.3 g white rhombic crystals separated out; m.p. 126-128°, readily soluble in chloroform, acetone and carbon tetrachloride; insoluble in water.

0.0428 g sub.: 0.635 ml 0.1 N H_2SO_4. 0.0312 g sub.: 0.897 ml 0.1 N $Na_2S_2O_3$. Found %: N 2.08; Sb 17.50. $C_{20}H_{18}ONSbHgCl_2$. Calculated %: N 2.05; Sb 17.89.

From 0.41 g triphenylantimonyacetimine dissolved in 5 ml chloroform and 2.56 ml 5% copper chloride solution was obtained 0.35 g white lamellar crystals which were washed with water and dried over calcium chloride in a desiccator. M.p. 138-140°. Readily soluble in chloroform, acetone, ethanol and carbon tetrachloride; insoluble in water.

0.0646 g sub.: 1.14 ml 0.1 N H_2SO_4 0.0574 g sub.: 2.12 ml 0.1 N $Na_2S_2O_3$. Found %: N 2.47; Sb 22.47. $C_{20}H_{18}ONSbCuCl_2$. Calculated %: N 2.57; Sb 22.37.

SUMMARY

1. The reaction of triphenylantimony with the sodium salt of N-bromoacetamide was studied.

2. Triphenylantimony was synthesized for the first time and its properties were described.

3. The composition of triphenylantimonyacetimine was confirmed by formation of derivatives with mercuric chloride and cooper chloride.

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QUINONES

VI. CONDENSATION OF p-BENZOQUINONE WITH α-AMINO ACIDS

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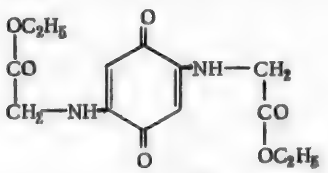
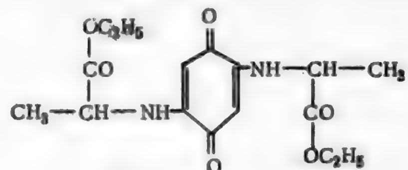
When quinones react with amino compounds, the amino nitrogen of the latter links up with carbon atoms of the quinone ring to form the corresponding derivatives of the mono- or diaminoquinone. Condensation products of this type were obtained by reacting quinones with various amines of both the aliphatic and aromatic series [1,2], including esters of α-amino acids [3,4]. Thus, for example, reaction of ethyl glycinate with p-benzoquinone gave the diester of diglycinoquinone (I), while the action of ethyl α-alaninate gave correspondingly the diester of dialaninoquinone (II) [3]:


(I)


(II)

Analogous products of condensation of quinones with free α-amino acids, however, have not up to now been described.

It was established that reaction of quinones with α-amino acids yields the aldehydes corresponding to the latter with one carbon atom less, and that the reaction is accompanied by release of carbon dioxide and ammonia [5,6,7]; the quinone is at the same time changed into hydroquinone. The process is evidently one of oxidative cleavage of the α-amino acids due to the lability of the hydrogen atom at the α-carbon atom. The mechanism of oxidative cleavage of α-amino acids may be represented by the scheme:

$$\underset{\displaystyle NH_2}{R-\underset{|}{CH}-COOH} \xrightarrow{O} \underset{\displaystyle NH}{R-\underset{\|}{C}-COOH} \xrightarrow{H_2O} NH_3 + CO_2 + R-CH{=}O.$$

In the reaction of α-amino acids with quinones, however, the oxidative cleavage of the acids does not by any means proceed quantitatively, and is possibly accompanied by condensation of the acids with quinones by the mechanism usual for quinones of type (I).

Such a direction of the reaction was first suggested by Cooper [8,9], who studied the kinetics of reaction of p-benzoquinone and toluquinone with various α-amino acids in dilute aqueous solutions and observed that these solutions acquire a deep-red color. Cooper suggested that the bearer of this color was also the product of condensation of the quinone with the amino acid. He did not, however, isolate any such condensation products; nor was their separation described in later publications on the reaction of α-amino acids with quinones [10].

In our experiments we studied the reaction of p-benzoquinone with glycine and α-alanine, and for the first time we succeeded in isolating the condensation products.

On pouring together heated aqueous solutions of quinone and glycine the reaction takes place with frothing due to oxidative cleavage of the amino acid, and an intense red color appears in the solution. At the same time, however, a dark-brown (nearly black) substance is precipitated whose quantity increases in the course of the reaction, and, especially when the temperature is raised, the red color of the solution disappears. This phenomenon alone prompted the idea that this red color, contrary to Cooper's suggestion, was not due to products of condensation of quinone with amino acid but to the presence of insignificant amounts of certain unstable substances, probably of a quinhydrone character. We obtained conclusive proof of the correctness of this theory by carrying out reactions relatively quickly at a low temperature in conditions facilitating development of the most intensive red color of the solution. On subsequently shaking the filtered aqueous solution with ether, the red color passed into the ethereal layer while the aqueous layer retained a brown color. From the aqueous layer, after evaporation and addition of ethanol, we isolated non-reacted glycine in the crystalline form. From the red ethereal solution,

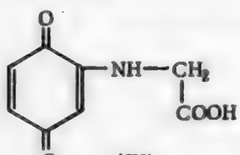
however, after drying and removal of the ether, we obtained a dry residue which only contained traces of nitrogen. This was identified as hydroquinone contaminated with insignificant amounts of colored impurities.

We found the product of condensation of p-benzoquinone with glycine in the precipitate resulting from heating of aqueous solutions of the starting components. The optimum yield was got by conducting the reaction at 50°.

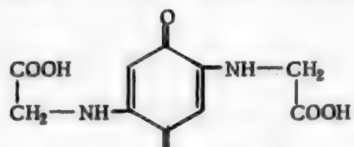
The substance formed is insoluble in water or ether. It is readily soluble in ethanol and acetic acid, but does not crystallize from these solvents. Dilution with water of the alcoholic or acetic acid solution of the substance precipitates it in the form of fine, dark-brown flocs. We used this method of purification of the substance.

The new compound is readily soluble in aqueous solutions of caustic alkalies or carbonates. Acidification of the alkaline solution brings down the substance in the form of fine, dark-brown flocs. Addition of hydrosulfite to the alkaline solution decolorizes it, but when the solution is then allowed to stand in contact with the air it again develops the brown color. This behavior points to the presence of a quinoid grouping in the compound. On dissolving the substance in an exactly calculated amount of water followed by addition of silver nitrate to the neutral solution, the water-insoluble silver salt comes down.

Quantitative determination of nitrogen in the thoroughly purified substance and of silver in the silver salt showed that the substance is the product of condensation of 1 molecule of p-benzoquinone with one molecule of glycine. Since the substance retains the quinoid grouping, the structure (III) should be assigned to it:



(III)



(IV)

When the reaction is carried out in the above-described optimum conditions, the yield of monoglycinoquinone (III) in relation to the glycine brought into reaction exceeds 50% of the theoretical. Bearing in mind that formation of glycinoquinone is also accompanied by oxidative cleavage of glycine, this yield must be regarded as fairly high.

In the reaction of p-benzoquinone with amino compounds the main product is usually, however, the diamino compound formed by introduction of two amino residues into the quinone molecule. Examples are the above-mentioned products of condensation of p-benzoquinone with glycine ester (I) and with α-alanyl ester (II). But the formation of products of condensation of one molecule of quinone with only one molecule of amino compound, similar to monoglycinoquinone (III), takes place in cases when with slow reaction the intermediately formed monoamino compound, which is insoluble in the reaction medium, separates as a precipitate, which is thereby removed from the sphere of the reaction. These conditions actually prevail during the interaction of p-benzoquinone with glycine in aqueous solution.

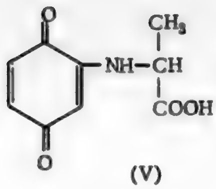
When the reaction is performed in ethanol, in which monoglycinoquinone (III) is soluble, the end product of reaction is diglycinoquinone (IV). Being poorly soluble in ethanol, diglycinoquinone is precipitated as formed, as a dark powder in a yield exceeding 30% in relation to the glycine brought into reaction.

Diglycinoquinone, like the monoglycino derivative, is soluble in aqueous alkalies and forms a stable, brown solution. Acidification of this solution brings down the diglycinoquinone unchanged. Addition to the sodium salt solution of silver nitrate brings down the water-insoluble silver salt.

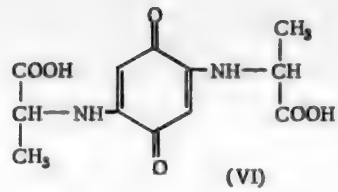
The composition of diglycinoquinone was confirmed by determination of the nitrogen content of the thoroughly purified product and of the silver content of its silver salt The structure of diglycinoquinone (IV) was confirmed by its preparation by saponification of the above-mentioned diethyl ester of diglycinoquinone (I), whose structure is not in doubt. Taking advantage of the relative stability of alkaline solutions of diglycinoquinone, we heated with 0.5 N sodium carbonate solution the ester of diglycinoquinone specially prepared from ethyl glycinate and quinone in accordance with the literature method [3]. The ester gradually went into solution, and acidification of the latter gave a diglycinoquinone identical in all its properties with the substance formed by reaction of p-benzoquinone with glycine in ethanolic solution.

Our experiments consequently showed that reaction of p-benzoquinone with glycine gives, apart from oxidative cleavage of the amino acid, products of condensation of the starting substances, monoglycinoquinone (III) and diglycinoquinone (IV).

Similarly in the reaction of p-benzoquinone with α-alanine there are formed, although in lower yields, monoalaninoquinone (V) in aqueous solution and dialaninoquinone (VI) in ethanolic solution.



(V)



(VI)

EXPERIMENTAL

I. Condensation of p-Benzoquinone with Glycine

Monoglycinoquinone

16.2 g benzoquinone (2 moles) was dissolved at 50° in 500 ml water. To this solution, with energetic stirring, was added dropwise a solution of 5.6 g glycine (1 mole) in 150 ml water at the same temperature. After the whole of the glycine solution had been added, the reaction mixture was stirred for 4 hours at 50° and then left overnight. By the next day it had completely lost its red color and had turned brown. The blackish-brown precipitate of monoglycinoquinone was filtered off, thoroughly washed with water, then with ether, and dried in the air. Yield 6.9 g (50.7% on the glycine). The aqueous mother liquor was shaken several times with ether; from the ethereal extract, after drying and removal of the ether, was obtained fairly pure hydroquinone; after two crystallizations from ether with addition of xylene, it melted at about 169°.

Monoglycinoquinone forms a black, friable powder. It is completely insoluble in cold water and nearly insoluble in hot; it is insoluble in ether, petroleum ether and ligroin. It is fairly easily soluble in ethanol and glacial acetic acid; dilution of the ethanolic or acetic acid solution with water precipitates it in the form of dark-brown flocs. On rapid heating in a capillary it melts with decomposition. It dissolves completely in dilute solution of sodium carbonate and sodium hydroxide, forming a brown solution of the sodium salt, from which it is again recovered by acidification with hydrochloric or sulfuric acid. If a weighed amount of monoglycinoquinone is exactly neutralized with a 2 N solution of NaOH (with transfer of a drop to phenolphthalein paper) and if silver nitrate solution is added to the obtained solution, the silver salt is formed. The latter forms a fine, very difficultly filterable, dark-brown precipitate; after thorough washing with water and drying at 60°, it forms a black powder with a metallic luster, completely insoluble in water.

Monoglycinoquinone is not modified by treatment with boiling dilute hydrochloric acid; it is also sufficiently stable to boiling with dilute caustic alkalies. Addition to the alkaline solution of monoglycinoquinone of sodium hydrosulfite with heating turns the solution light-yellow; on shaking in contact with the air it again oxidizes and darkens.

0.1278, 0.1628 g sub.: 6.69, 8.63 ml 0.1 N H_2SO_4 (Kjeldahl). Found %: N 7.35, 7.42. $C_8H_7O_4N$. Calculated %: N 7.73.

A weighed sample of the silver salt was boiled in a Kjeldahl flask with 10 ml conc. HNO_3 (d 1.45) until completely decolorized. The AgCl was then precipitated as usual.

0.2241, 0.1944 g sub.: 0.1128, 0.0980 g AgCl. Found %: Ag 37.84, 37.96. $C_8H_6O_4NAg$. Calculated %: Ag 37.47.

Diglycinoquinone

8.1 g benzoquinone (3 moles) was dissolved in 200 ml ethanol. The solution was heated to 50° and addition was made, dropwise with energetic stirring, of a solution of 3.8 g glycine (2 moles) in 20 ml water. Heating was continued for 2 hours, after which the reaction mixture was left overnight. The next day, the black, easily filterable precipitate of diglycinoquinone was filtered from the brown ethanolic mother liquor, thoroughly washed with ethanol and ether, and dried in the air. Yield 2 g (31.3%). The ethanolic mother liquor was diluted with a large quantity of water to precipitate the monoglycinoquinone. The latter was filtered and washed with water and ether. After air-drying, weight 1.7 g.

Diglycinoquinone forms a black, friable, microcrystalline powder, outwardly resembling monoglycinoquinone. Unlike the latter, it is substantially insoluble in ethanol. It dissolves with difficulty in glacial acetic acid. When heated in a capillary it decomposes without melting. It dissolves completely in dilute solutions of sodium carbonate and NaOH, forming, like monoglycinoquinone, a solution of the sodium salt from which it can

again be precipitated by acidification. Addition of $AgNO_3$ solution to the sodium salt solution gives the insoluble silver salt of diglycinoquinone. The latter was analyzed in the following manner: 0.98 g diglycinoquinone, thoroughly washed with ethanol, was dissolved in 78.7 ml (2 equivs.) of exactly 0.1 N NaOH, and to the obtained solution was added a solution of 1.31 g (2 equivs.) $AgNO_3$ in 50 ml water. The next day the precipitated silver salt was filtered, washed with water, alcohol and ether and dried at 120°. It was then in the form of a black powder with a metallic luster. Diglycinoquinone is not modified by treatment with boiling dilute HCl; it is quite stable in boiling dilute alkalies.

0.1036, 0.1196 g sub.: 8.96, 9.87 ml 0.1 N H_2SO_4 (Kjeldahl). Found %: N 11.33, 11.56. $C_{10}H_{10}O_6N_2$. Calculated %: N 11.02.

Analysis of silver salt for silver:

0.2396, 0.2129 g sub.: 0.1535, 0.1324 g AgCl. Found %: Ag 46.56, 46.87. $C_{10}H_8O_6N_2Ag_2$. Calculated %: Ag 46.15.

Preparation of Diglycinoquinone by Saponification of its Diethyl Ester

2 g diethyl ester of diglycinoquinone (m.p. 210°), prepared by condensation of benzoquinone with ethyl glycinate [3], was introduced into 48 ml 0.5 N Na_2CO_3. The mixture was heated on a water bath to complete solution of the ester. The brown-red solution was filtered and then acidified with 10% HCl to an acidic reaction. The precipatated diglycinoquinone was filtered, washed with hot water and ethanol, and dried at 120°. Yield 0.5 g (30.5%).

The diglycinoquinone was identical in all properties with the compound synthesized by condensation of benzoquinone with glycine.

0.0906, 0.0748 g sub.: 7.12, 5.92 ml 0.1 N H_2SO_4 (Kjeldahl). Found %: N 11.02, 11.07. $C_{10}H_{10}O_6N_2$. Calculated %: N 11.02.

II. Condensation of p-Benzoquinone with α-Alanine

Monoalaninoquinone

5.4 g (2 moles) benzoquinone was dissolved at 50° in 200 ml water. To the solution was added dropwise, with vigorous stirring, a solution of 2.2 g (1 mole) alanine in 50 ml water and the mixture was stirred at the same temperature for 6 hours. The next day the precipitated monoalaninoquinone was filtered from the brown mother liquor, repeatedly washed with hot water, then with ether, and dried. Yield 1.2 g (25 %). For analysis the substance was reprecipitated from ethanolic (or alkaline) solution.

Monoalaninoquinone forms a black powder, similar in properties to monoglycinoquinone.

0.1190, 0.1480 g sub.: 6.33, 7.71 ml 0.1 N H_2SO_4 (Kjeldahl). Found %: N 7.30, 7.22. $C_9H_9O_4N$. Calculated %: N 7.18.

Dialaninoquinone

To a solution of 8.1 g (3 moles) benzoquinone in 300 ml ethanol, heated to 60°, was added dropwise with vigorous stirring a solution of 4.4 g (2 moles) alanine in 50 ml water. Stirring and heating were continued for 9 hours, after which the mixture was left overnight at room temperature. The next day the precipitate of dialaninoquinone, appreciably contaminated with unreacted alanine, was filtered from the dark-brown mother liquor, washed with hot ethanol, then with water, once again with ethanol and finally with ether. The precipitate was detached from the filter and ground in a mortar; it was covered with ethanol and left for several hours. Then the dialaninoquinone was filtered again and washed with ethanol until a perfectly colorless filtrate ran through the funnel. Yield 1 g (15%). For analysis the dialaninoquinone was reprecipitated from alkaline solution, washed with water and dried at 120°. Dialaninoquinone is a black powder. Unlike monoalaninoquinone it is insoluble in ethanol. Its properties are similar to those of diglycinoquinone.

0.1244, 0.1152 g sub.: 8.43, 8.11 ml 0.1 N H_2SO_4 (Kjeldahl). Found %: N 9.34, 9.48. $C_{12}H_{14}O_6N_2$. Calculated %: N 9.90.

SUMMARY

Reaction between p-benzoquinone and α-amino acids results, apart from the oxidative cleavage of the amino acids described in the literature, in formation of products of condensation of the acids with p-benzoquinone of the type usual for quinones.

From p-benzoquinone and glycine were obtained mono- and diglycinoquinones; correspondingly, p-benzoquinone with α-alanine yielded mono- and dialaninoquinones.

Products of condensation of 1 molecule of p-benzoquinone with 1 molecule of amino acid are obtained by carrying out the reaction in aqueous solution; since they are insoluble in water they are precipitated. Products of condensation of 1 molecule of quinone with two molecules of amino acid were obtained by carrying out the reaction in ethanolic solution.

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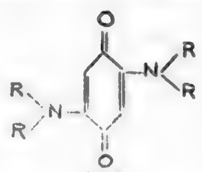
QUINONES

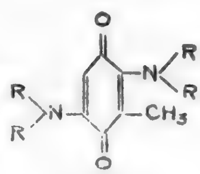
VII. REACTION OF CHLORO DERIVATIVES OF p-BENZOQUINONE WITH ETHYL GLYCINATE

I.S. Ioffe and Z.Ya. Khavin

In the preceding communication [1] we considered the reaction of p-benzoquinone with amino compounds leading to addition of amino radicals to carbon atoms of the quinoid nucleus. This reaction usually culminates in the formation of diamino derivatives of the quinone containing both amino groups, as a rule, in the p-position to one another. The compounds are of the general type (I):



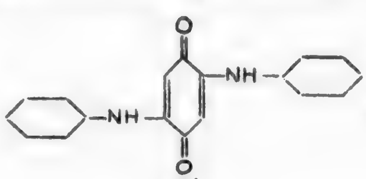
(I)



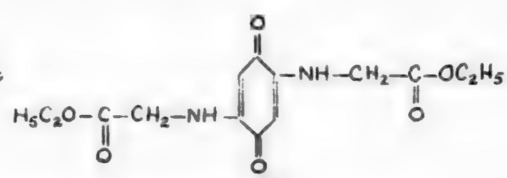
(II)

Like benzoquinone, toluquinone also adds on two amino groups with formation of compounds of type (II). The methyl group has no appreciable influence upon the course of the reaction. On reaction of amines with chloroquinones [2,3,4], however, amino radicals not only add on to the unsubstituted carbon atoms but they also displace the chlorine atoms. Literature data on this subject, however, are contradictory. According to one report [2] treatment of chloroquinone with amines gives chlorine-free diaminoquinones, whereas elsewhere [3] the formation of chlorodiaminoquinones is reported. Again, trichloroquinone is reported [3] to lose one chlorine atom to form dichlorodiaminoquinones, while other workers [4] claim to displace two atoms of chlorine to obtain monochlorodiaminoquinones.

This problem has been studied most closely by Niemeyer [2] who condensed various quinones with aniline and toluidine. All the products that he obtained by this condensation, however, resemble dianilinoquinone (III) in being poorly soluble in organic solvents, in not being readily amenable to purification by crystallization, and in melting unsharply at above 300°. Niemeyer was, therefore, unable to accurately establish the course of the reaction of chloroquinones with amines.



(III)



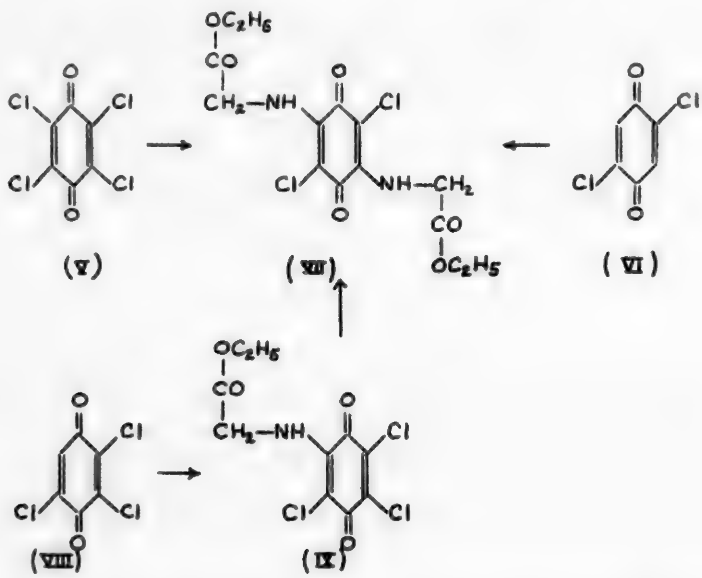
(IV)

Of the diamino derivatives of quinone, the product of condensation with ethyl glycinate (IV) [5], described in the preceding communication [1], is distinguished by the ability to crystallize well from organic solvents, by high stability, and by the relatively low and sharp m.p. of 210°; we, therefore, carried out the condensation of ethyl glycinate with various chloroquinones. By carrying out this reaction in a variety of conditions, we were able, moreover, to segregate the introduction of amino radicals at unsubstituted carbon atoms of the quinoid nucleus from the displacement of chlorine atoms by amino groups, and, thereby, were able to compare both of these directions of the reaction.

The reaction proceeds the most smoothly with tetrachloroquinone (V). On mixing solutions, heated to 60°, of ethyl glycinate and tetrachloroquinone in ethyl acetate, a violet-red color is developed whose intensity increases with further heating. On cooling, a precipitate comes down and consists of a mixture of glycine hydrochloride and the product of condensation of the starting components. The product was purified by crystallization from ethyl acetate and separated in the form of brick-red clusters with constant m.p. of 199-120°.

Analysis showed that this substance contains two chlorine atoms and two ethyl glycinate residues. The relative positions of the substituents was established by the observation that the identical substance is obtained on condensing ethyl glycinate with 2,5-dichloroquinone (VI). Hence, the reaction of tetrachloroquinone with the amine results in displacement of the two atoms of chlorine in the p-position to one another, and the product is the diethyl ester of 2,5-dichloro-3,6-diglycinoquinone with the structure (VII).

The mode of formation of this dichlorodiaminoquinone (VII) from tetrachloroquinone differs fundamentally, however, from the mode of formation from 2,5-dichloroquinone. With 2,5-dichloroquinone the reaction follows the course usual for quinones, the amino residues adding onto the unsubstituted carbon atoms of the quinoid nucleus; this reaction takes place quickly at a moderate temperature. In the reaction with tetrachloroquinone, however, 2 amino residues displace 2 chlorine atoms in the p-position to one another. Heating is needed to speed up this reaction.

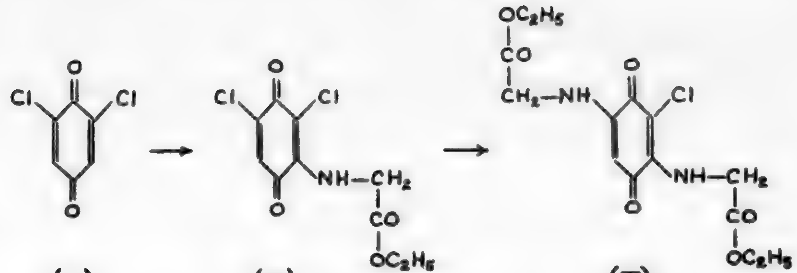


(V) (VII) (VI)

(VIII) (IX)

When ethyl glycinate reacts with trichloroquinone (VIII) the reaction proceeds in both of the above-described directions. At first an amino residue adds on to the sole unsubstituted carbon atom of the trichloroquinone molecule with formation of the ester of trichloroglycinoquinone (IX). At the same time, however, displacement of one of the chlorine atoms by still another amino residue takes place. The resultant product melts at 199-200° and is identical with the above-described diester of dichlorodiglycinoquinone (VII). From this it follows that also in the present case an amino residue displaces a chlorine atom in the p-position to the initially introduced amino group. When the reaction is carried out in the cold, it is possible to obtain a mixture of both products of condensation. Of these the ester of trichloroglycinoquinone (IX) is distinguished by its greatly superior solubility; it can be isolated only in insignificant yield. It crystallizes from ethanol-ligroine mixture in the form of dark-red needles with m.p. 111-112°. With more prolonged reaction or when the mixture is heated, the sole product of condensation is the diester of dichlorodiglycinoquinone (VII) with m.p. 199-200°.

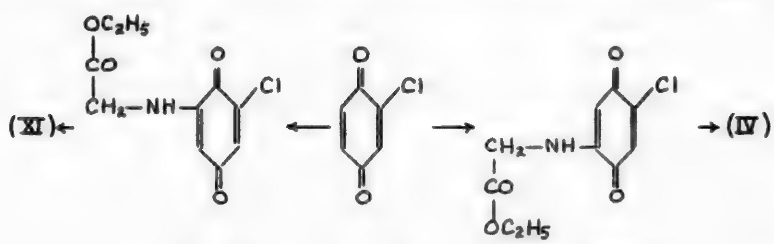
Mixing of the ethyl acetate solutions of 2,6-dichloroquinone (X) and ethyl glycinate gave a condensation product whose analysis revealed the presence of 1 chlorine atom and 2 amino residues; it was evidently the diester of 2-chloro-3,6-diglycinoquinone (XI). This substance is poorly soluble in ethyl acetate and crystallizes as bright-red clusters with constant m.p. of 189-190°. As in the case of reaction with trichloroquinone, the formation of this substance involves addition of an amino residue to one of the equivalent unsubstituted carbon atoms of the 2,6-dichloroquinone molecule and displacement of an atom of chlorine in the p-position to this amino group by another amino residue. Our observations reveal that also in this case the addition of the amino residue to the unsubstituted carbon atom with formation of the ester of 2,6-dichloro-3-glycinoquinone (XII) proceeds with a higher velocity, but we were unable to obtain this intermediate product in the pure form. During the reaction it changes into the diamino derivative (XI). When the reaction is carried out for a short period in the cold, however, the amount of monoamino derivative (XII) formed is small; it is very soluble in organic solvents and even in water; hence attempts to isolate this substance and to crystallize it were unsuccessful.



(X) (XII) (XI)

The course of the reaction of ethyl glycinate with monochloroquinone (XIII) was more complex. Mixing and moderate heating of ethyl acetate solutions of these substances results in precipitation of a dark-red chlorine-containing product. In different experiments its m.p. varied between 180 and 190°. It crystallizes from ethyl acetate but the m.p. of the crystals is not constant; in some experiments it reaches 200°. No marked depression of melting point was observed on mixing either with the chlorine-free diester of the diglycinoquinone (IV) with m.p. 210° or with the diester of 2-chloro-3,6-diglycinoquinone (XI) with m.p. 189-190°. Analytical determinations of chlorine and amino nitrogen in the repeatedly crystallized product show thatis a mixture of compounds (IV) and (XI) which is not amenable to resolution in the conditions employed by us.

Formation of both of these substances on reaction of chloroquinone with ethyl glycinate can be explained in the following manner. At first an amino residue must add on to one of the unsubstituted carbon atoms of (XIII). Under the dual electronic influence of the halogen, the amino group can enter both in the p-position to the chlorine with formation of 2-chloro-5-aminoquinone (XIV) and in the m-position with formation of 2-chloro-6-aminoquinone (XV). Each of these intermediately formed substances, however, can easily take up another amino residue but now, as a rule, in the p-position to the original amino group. For 2-chloro-5-aminoquinone (XIV) this reaction proceeds with displacement of the halogen and with formation of the halogen-free diester of diglycinoquinone (IV). In the 2-chloro-6-amino compound (XV) the amino group adds on to the unsubstituted carbon atom in the 3-position with formation of the diester of 2-chloro-3,6-diglycinoquinone (XI). The mixture of these substances is also the end product of the reaction of chloroquinone with ethyl glycinate:



(XV) (XIII) (XIV)

Our results and the considerations advanced in the course of their evaluation allow us to clear up the conflicting statements in the literature. Our observations on the reaction of chloroquinones with ethyl glycinate are also in accord with some special cases of condensation of chloroquinones with amines described in the literature [6-10].

EXPERIMENTAL

Reaction of Tetrachloroquinone

3 g (1 mole) tetrachloroquinone was dissolved at 60° in 225 ml ethyl acetate. To the solution at the same temperature was added a solution of 2.5 g (2 moles) ethyl glycinate in 10 ml ethyl acetate. The mixture of solutions acquired a violet-red color. After standing and cooling, the diester of dichlorodiglycinoquinone came down in admixture with samll white needles of ethyl glycinate hydrochloride. The condensation product was extracted with boiling ethyl acetate in which ethyl glycinate hydrochloride is substantially insoluble.

Cooling of the filtered, hot solution brought down the diester of dichlorodiglycinoquinone in quantity of 2.3 g or 50% of the theoretical yield. It forms clusters with a characteristic, somewhat whitish, brick-red color. After repeated crystallization its m.p. is constant at 199-200°.

0.1710, 0.1606 g sub.: 0.1298, 0.1204 g AgCl. Found %: Cl 18.79, 18.56. $C_{14}H_{16}O_6N_2Cl_2$. Calculated %: Cl 18.73.

Reaction of 2,5-Dichloroquinone

4 g (3 moles) 2,5-dichloroquinone was dissolved with heating in 70 ml ethyl acetate. When all had dissolved, the solution was carefully cooled to 40-50° before adding a solution of 1.8 g (2 moles) ethyl glycinate in 10 ml ethyl acetate. The mixture was vigorously stirred. The solution acquired a deep-red color with a brownish tinge and soon began to deposit crystals of condensation product. After a few hours these were filtered, washed with ethyl acetate and dried in the air; yield of diester of dichlorodiglycinoquinone 1.9 g (67%). After several crystallizations from ethyl acetate the compound has a sharp m.p. of 199-200°. A mixed test with the compound obtained from tetrachloroquinone melts at 199-200°.

0.1715, 0.1695 g sub.: 0.1274, 0.1272 g AgCl. Found %: Cl 18.40, 18.58. $C_{14}H_{16}O_6N_2Cl_2$. Calculated %: Cl 18.73.

Reaction of Trichloroquinone

a) To a solution of 3 g (2 moles) trichloroquinone in 40 ml ethyl acetate, heated to boiling, was added 2 g (3 moles) ethyl glycinate in 15 ml ethyl acetate; the mixture acquired a dark-red color. Cooling brought down a mixture of condensation product and ethyl glycinate hydrochloride. Extraction with ethyl acetate yielded 1.36 g of the diester of dichlorodiglycinoquinone (50.4%). After the first crystallization the substance melted at 185-188°; after the second at 199-200°. A mixed test with the substance obtained from tetrachloroquinone and from 2,5-dichloroquinone melted at 199-200°.

0.1685, 0.1532 g sub.: 0.1260, 0.1154 g AgCl. Found %: Cl 18.51, 18.65. $C_{14}H_{16}O_6N_2Cl_2$. Calculated %: Cl 18.73.

b) 5 g (2 moles) trichloroquinone was dissolved in 100 ml ethyl acetate and the solution was cooled with ice and salt; with vigorous stirring dropwise addition was made of a solution of 1.2 g (1 mole) ethyl glycinate in 30 ml ethyl acetate. The dark-cherry solution was kept for another 3-4 hours(cooled with iced water) and then left overnight at room temperature. In the solution was found only an insignificant deposit which was filtered off. The ethyl acetate was driven off from the cherry-red filtrate in vacuum, and the residue was dried in a vacuum-desiccator.

Fractional crystallization from alcohol enabled separation of the condensation product – the ester of trichloroglycinoquinone – from the considerably less soluble trichlorohydroquinone. It was recrystallized from alcohol-ligroine mixture. The yield was very low (0.9 g). Dark-red needles with m.p. 111-112°.

0.1126 g sub.: 0.1414 g AgCl. Found %: Cl 31.09. $C_{10}H_8O_4NCl_3$. Calculated %: Cl 34.08.

Reaction of 2,6-Dichloroquinone

A solution of 3.3 g (2 moles) 2,6-dichloroquinone in 50 ml ethyl acetate was poured with energetic stirring into a solution of 3 g (3 moles) ethyl glycinate in 15 ml ethyl acetate. On mixing heat was evolved and the solution became dark cherry-red. With continued stirring the color changed to brown and a brick-red precipitate of the condensation product – the diester of chlorodiglycinoquinone – separated from the solution. After keeping overnight, it was filtered off, washed with cold ethyl acetate and dried. Yield 3 g (94%). Very sparingly soluble in ethyl acetate, almost insoluble in ethanol and ether. After recrystallization from excess of boiling ethyl acetate it formed very beautiful, bright-red, lustrous clusters with sharp m.p. of 189-190°.

0.1518, 0.1629 g sub.: 0.0631, 0.0679 g AgCl. Found %: Cl 10.28, 10.32. $C_{14}H_{17}O_6N_2Cl$. Calculated %: Cl 10.30.

SUMMARY

The reaction of chloroquinones with amines culminates, like the reaction with the unsubstituted quinone, in formation of the diamino derivative of the quinone containing, as a rule, both amino groups in the p-position to one another. Depending upon the number of halogen atoms and their relative positions, this reaction proceeds according to two different mechanisms in two directions involving respectively addition of amino residues to the unsubstituted carbon atoms of the quinoid nucleus and displacement of halogen atoms by amino residues.

The amino residues add on to the unsubstituted carbon atoms of the quinoid nucleus with greater velocity and in milder conditions. If the carbon atoms in the p-position to one another are free, then amino residues add on to both. If a chlorine atom is attached to the carbon atom in the p-position to the added-on amino residue, then the chlorine atom is displaced by another amino residue. Chlorine atoms in the o- and m-positions to the

amino group are stable. In tetrachloroquinone 2 chlorine atoms in the p-position to one another are displaced by amino residues.

Consequently one and the same 2,5-dichloro-3,6-diamino derivative is formed from 2,5-dichloroquinone, trichloroquinone and tetrachloroquinone; 2,6-dichloroquinone gives the 2-chloro-3,6- derivative; from monochloroquinone, where intermediate addition of an amino residue is possible in both the p- and m-position to the chlorine, the end product of the reaction is a mixture of 3,6-diaminoquinone and the 2-chloro-3,6-diamino derivative.

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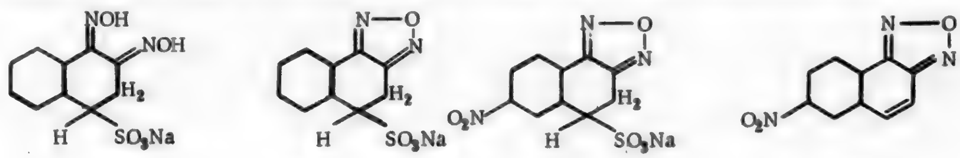
INVESTIGATIONS IN THE 1,2-NAPHTHO-(3',4')-FURAZAN SERIES

III. THE BISULFITE COMPOUND OF 1,2-NAPHTHO-(3',4')-FURAZAN AND 6-NITRO-1,2-NAPHTHO-(3',4')-FURAZAN

S.V. Bogdanov and S.F. Petrov

It has been observed [1] that boiling of the bisulfite compound 1,2-naphthoquinonedioxime (I) with sodium carbonate solution converts it into 1,2-naphtho-(3',4')-furazan (1,2-naphthoquinonedioxime anhydride). It appeared probable that the first step in the reaction is scission of the bisulfite compound into sulfite and 1,2-naphthoquinonedioxime, and the second step the dehydration of naphthoquinonedioxime to naphthofurazan. The bisulfite compound actually undergoes scission in this manner with sodium hydroxide. On the other hand we cannot exclude the possibility of preliminary dehydration of the bisulfite compound of naphthoquinonedioxime to the bisulfite compound of naphthofurazan followed by cleavage of bisulfite. Experiments showed that heating of a solution of the bisulfite compound of naphthoquinonedioxime with a very slight excess of sodium carbonate at 60-100° actually led to the bisulfite compound of 1,2-naphtho-(3',4')-furazan (II). Further treatment of this bisulfite compound with sodium carbonate or sodium hydroxide splits it into sulfite and naphthofurazan. In an acid medium the bond between sulfurous acid and the naphthofurazan molecule is so strong that when the bisulfite compound of naphthofurazan in sulfuric acid solution is treated with nitric acid, it is converted into the nitro compound without cleavage of sulfurous acid. Whereas the main products of nitration of free 1,2-naphtho-(3',4')-furzan are 5- and 7-nitronaphthofurazans [2], substitution here occurs mainly in the 6-position. The resultant bisulfite compound of 6-nitro-1,2-naphtho-(3',4')-furazan (III) is converted by the action of caustic alkali into 6-nitronaphthofurazan (IV), while its reduction gives the bisulfite compound of aminonaphthofurazan.



(I) (II) (III) (IV)

The structure of 6-nitronaphthofurazan was established by its conversion into 6-aminonaphthofurazan and then (via the diazo compound) into naphthofurazan-6-sulfonic acid; also by comparison with the naphthofurazan-6-sulfonic acid obtained from 1-nitroso-2-naphthol-6-sulfonic acid via 1,2-naphthoquinonedioxime-6-sulfonic acid [3].

The diazo compound from 6-aminonaphthofurazan was also transformed into 6-chloro- and 6-hydroxynaphthofurazan.

Attempts to prepare the bisulfite compound of naphthofurazan by treatment of naphthofurazan with 5 times the quantity of bisulfite in an aqueous ethanolic medium by boiling or by heating in a tube at 170° were unsuccessful.

EXPERIMENTAL

Bisulfite Compound of 1,2-naphtho-(3',4')-furazan. Into 73 ml sodium carbonate solution containing 5.4 g sodium carbonate was introduced at 20° 27 g of the sulfite of 1,2-naphthoquinonedioxime. The solution was boiled for an hour and then cooled. The grey bisulfite compound was filtered and washed with water, ethanol and ether; yield 24.2 g (73.8%).

On adding the sulfite compound to a solution of sodium carbonate heated to 60 or 70° and holding the solution for 2 hours at the same temperature, the yield of bisulfite compound of naphthofurazan was 7.8 and 16.78 g. Small amounts of naphthofurzan were formed in all the experiments. The colorless rectangular plates (from aqueous ethanol) are readily soluble in water, insoluble in organic solvents.

0.9967 g sub.: loss on drying (170°) 0.1635 g. 0.2560 g dry. sub.: 0.0662 g Na_2SO_4. 6.814 mg sub.: 9.150 mg CO_2; 2.404 mg H_2O. 2.917 mg sub.: 0.236 ml N_2 (30°, 725 mm). Found %: H_2O 16.40; Na 8.37; C 36.64; H 3.95; N 8.70. $C_{10}H_7O_4N_2SNa \cdot 3H_2O$. Calculated %: H_2O 16.46; C 36.58; H 3.99; N 8.53. $C_{10}H_7O_4N_2SNa$. Calculated %: Na 8.39.

Nitration of the bisulfite compound. To a solution of 18.25 g (0.0666 mole) bisulfite compound (dried at 170°) in 125 ml conc. sulfuric acid was added, at -2°, a mixture of 4.37 g (0.0687 mole) 99.1% nitric acid and 26 ml sulfuric acid in the course of an hour. The reaction mass was stirred 2 hours and poured into 1500 g ice. The solution was neutralized with calcium carbonate, the calcium sulfate was filtered off, and the filtrate evaporated to dryness. For removal of traces of gypsum the residue was treated with a small amount of hot water, and the solution was filtered and again evaporated to dryness. Weight of residue (dried at 150°) 21.6 g; it was a mixture of the sodium salt and a small amount of calcium salt. This mixture was treated with 220 ml boiling ethanol and the calcium salt filtered off; weight of latter (dried at 150°) 1.3 g. Colorless, short prisms (from water), poorly soluble in cold water and readily in hot water, very sparingly soluble in ethanol.

0.3372 g sub.: loss on drying (170°) 0.0414 g. 7.934 mg sub.: 9.642 mg CO_2; 2.330 mg H_2O. 2.752 mg sub.: 0.292 ml N_2 (29°, 726 mm). Found %: H_2O 12.27; C 33.16; H 3.29; N 11.47. $C_{20}H_{12}O_{12}N_6S_2Ca \cdot 5H_2O$ Calculated %: H_2O 12.47; C 33.24; H 3.07; N 11.63.

Partial evaporation of the filtrate from the calcium salt led to separation of 13.5 g (after drying at 150°) sodium salt of the bisulfite compound.

Long colorless prisms (from ethanol), readily soluble in water, less soluble in ethanol.

0.41 38 g sub.: loss on drying (170°) 0.0425 g. 6.684 mg sub.: 8.252 mg CO_2; 1.690 mg H_2O. 3.410 mg sub.: 0.370 ml N_2 (22°, 729 mm). Found %: H_2O 10.27; C 33.67; H 2.83; N 12.04. $C_{10}H_6O_6N_3SNa \cdot 2H_2O$. Calculated %: H_2O 10.14; C 33.80; H 2.84; N 11.82.

When the calcium and sodium salts of the bisulfite compound are heated with 0.5 N NaOH, they break down with formation of 6-nitronaphthofurazan and sulfite. 6-Nitronaphthofurazan crystallizes from acetic acid in the form of needles, m.p. 202.7-203.7°, readily soluble in acetic acid and very much less soluble in ethanol.

3.483 mg sub.: 0.613 ml N_2 (21°, 730 mm). Found %: N 19.63. $C_{10}H_5O_3N_3$. Calculated %: N 19.54.

On further evaporation of the filtrate from the calcium salt, further separation was effected of 6.11 g bisulfite compound. Caustic alkali imparts a dark-brown color to its solution and a yellow precipitate is separated with m.p. 165-177°. It could not be resolved into its components. Judging by the results of reduction of this mixture, its main component was 6-nitronaphthofurazan.

6-Aminonaphthofurazan a) Into a solution of 5.33 g sodium salt of the bisulfite compound of nitronaphthofurazan in 50 ml water, acidified with 0.25 ml 60% acetic acid, was introduced 2.2 g iron filings at 75° in the course of 30 minutes; the mixture was then held at 75° for 1 and a half hours. After addition of magnesia, the sludge was filtered off, the filtrate was evaporated to dryness, and the residue was crystallized from water; yield 0.77 g. The bisulfite compound of aminonaphthofurazan forms greenish needles, readily soluble in water and less readily in ethanol. Heating with 5% NaOH liberates the free amino compound with m.p. 172.8-173.1°.

b) 6-Nitronaphthofurazan was reduced on the same lines as the product of nitration of naphthofurazan [2].

Using Fe turnings 8.6 g (0.04 mole) nitro compound gave 6.7 g aminonaphthofurazan with m.p. 172.1-172.8°. Using sodium sulfite as reducing agent, 1.85 g nitro compound gave 0.96 g amino compound with m.p. 170.9-171.8° and 0.45 g by-product insoluble in hydrochloric acid. Yellow needles (from ethanol) with m.p. 173.1-173.7°, readily soluble in ethanol and benzene.

3.275 mg sub.: 0.665 ml N_2 (24°, 735 mm). Found %: N 22.57. $C_{10}H_7ON_3$. Calculated %: N 22.70.

The hydrochloride (from 4% hydrochloric acid) forms colorless needles, considerably more stable than the salts of 5- and 7-aminonaphthofurazans.

6-Chloronaphthofurazan. To a suspension of 1.85 g (0.01 mole) 6-aminonaphthofurazan in 120 ml 4% HCl at 0-5° was added a solution of 0.76 g sodium nitrite in 20 ml water. The solution of the diazo compound was run into a solution (heated to 70-80°) of 3.2 g cuprous chloride in 48 ml 36% HCl and 16 ml water. After stirring for 30 minutes at 70-80°, the mixture was cooled, and the chloronaphthofurazan was filtered off; yield 1.83 g. Colorless needles (from isobutyl alcohol), m.p. 148-148.3°. Dissolves readily in ethanol, isobutyl alcohol, chlorobenzene and acetic acid.

3.061 mg sub.: 0.383 ml N_2 (31°, 734 mm). Found %: N 13.57. $C_{10}H_5ON_2Cl$. Calculated %: N 13.70.

6-Hydroxynaphthofurazan. Preparation was by the same procedure as for 7-hydroxynaphthofurazan [2] from 2.77 g 6-aminonaphthofurazan; yield 2.19 g.

Light-yellow needles (from methanol), m.p. 190.2-190.9°. Readily soluble in organic solvents.

3.777 mg sub.: 0.510 ml N_2 (21°, 730 mm). Found %: N 15.06. $C_{10}H_6O_2N_2$. Calculated %: N 15.05.

Naphthofurazan-6-sulfonic acid a) A sulfuric acid solution of the diazo compound prepared from 3.33 g 6-aminonaphthofurazan was treated as already described for 5-diazonaphthofurazan [2]. Yield of sodium salt of the sulfonic acid 4.15 g. Colorless rhombic plates (from water), readily soluble in water.

0.2700 g substance: loss on drying (120°) 0.0316 g. 0.2693 g dry sub.: 0.0703 g Na_2SO_4. Found %: H_2O 11.70; Na 8.45. $C_{10}H_5O_4N_2SNa \cdot 2H_2O$. Calculated %: H_2O 11.69. $C_{10}H_5O_4N_2SNa$. Calculated %: Na 8.45.

Sulfochloride. Elongated rhombic plates (from chlorobenzene), m.p. 202.2-202.3°.

Amide. Needles (from chlorobenzene), m.p. 245. 8-246.5°.

2.851 mg sub.: 0.438 ml N_2 (27°, 728 mm). Found %: N 16.75. $C_{10}H_7O_3N_3S$. Calculated %: N 16.86.

b) A solution of 36.2 g (0.1 mole) sodium salt of 1,2-naphthoquinonedioxime-6-sulfonic acid in 320 ml 10% NaOH solution was boiled for an hour and cooled. The separated sodium salt of naphthofurazan-6-sulfonic acid was filtered; yield 29.48 g.

Sulfochloride. Elongated rhombic plates (from chlorobenzene), m.p. 202.8-203.7°. Melting point of mixture of sulfochlorides 202.5-203.4°.

Amide. Needles (from chlorobenzene), m.p. 246-247°. Melting point of mixture of amides 246-246.7°.

SUMMARY

1. Heating of a solution of the bisulfite compound of 1,2-naphthoquinonedioxime with a small quantity of sodium carbonate gives the bisulfite compound of 1,2-naphtho-(3',4')-furzan.

2. The bisulfite compound of 1,2-naphtho-(3',4')-furazan is converted on nitration into the bisulfite compound of 6-nitro-1,2-naphtho-(3',4')-furazan.

3. From 6-nitro-1,2-naphtho-(3',4')-furazan was obtained 6-amino-1,2-naphtho-(3',4')-furazan; from the latter were obtained 6-chloro-1,2-naphtho-(3',4')-furazan, 6-hydroxy-1,2-naphtho-(3',4')-furazan, and 1,2-naphtho-(3',4')-furazan-6-sulfonic acid.

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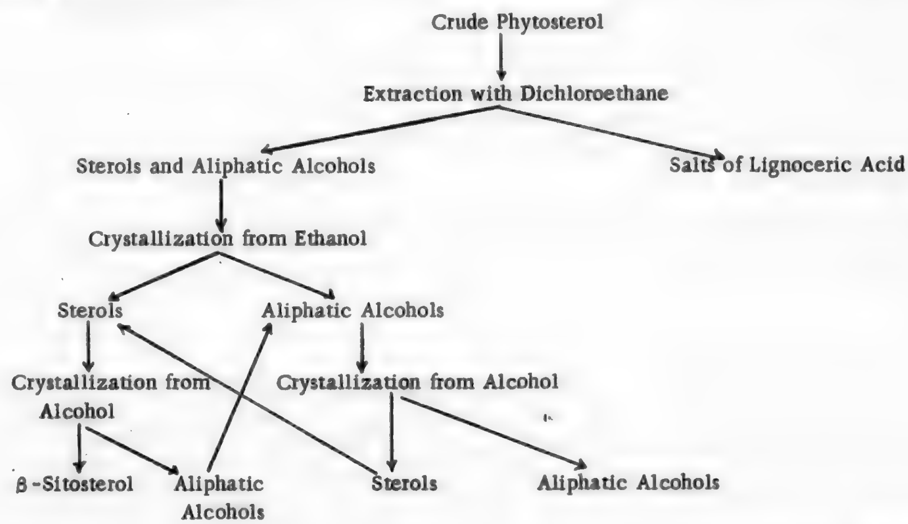
* See Consultants Bureau Translation, p. 395.

ISOLATION OF β-SITOSTEROL FROM CRUDE PHYTOSTEROL AND ITS ANALYSIS

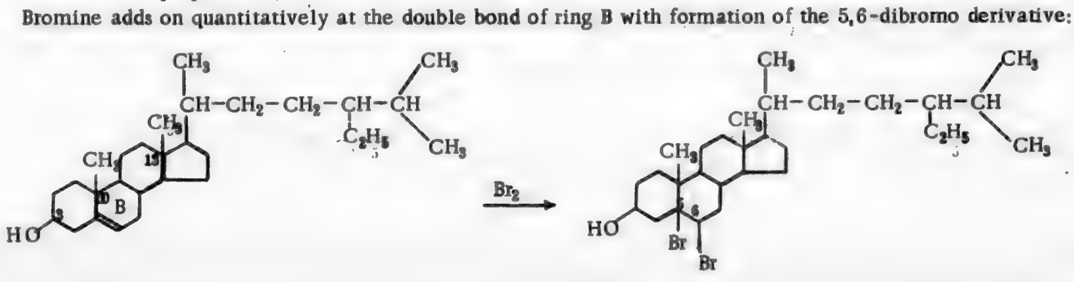
A.M. Khaletsky and I.M. Yurist

In the preceding investigation [1] it was shown that crude phytosterol, obtained by alkaline hydrolysis of pinewood, is a mixture of sterols, higher aliphatic alcohols and salts of higher molecular acids, the predominant components being β-sitosterol, lignoceryl alcohol, and salts of lignoceric acid. It was of interest to establish convenient methods of isolation of β-sitosterol with avoidance under industrial conditions of extraction of crude phytosterol with ether and of benzoylation of the isolated sterols. Numerous experiments led to the conclusion that extraction of sterols and aliphatic alcohols with ether may be replaced by extraction with dichloroethane, while β-sitosterol could be separated from sterols by recrystallization from alcohol according to the scheme given below.

In working up large amounts of crude phytosterol, it is expedient to crystallize the fraction containing the sterols and aliphatic alcohols from the mother liquor remaining after a second crystallization of the sterols, and to add the separated sterols to those previously isolated and to crystallize them from ethanol. In this manner isolation was effected from crude phytosterol of about 30% β-sitosterol with m.p. 134-136°, over 40% of the aliphatic alcohols in admixture with other sterols, and over 20% of the salts of lignoceric acid; about 10% consisted of inorganic substances and moisture. The β-sitosterol isolated from crude phytosterol merits interest in that in its molecule the spatial arrangement of the rings and of the individual groups (angular methyl groups at C_{10} and C_{13} and secondary alcoholic grouping at C_3, as well as the double bond at $C_5—C_6$) is the same as in chloesterol, only differing in that at C_{24} there is an additional alkyl group - C_2H_5 [2]. Not less interest is presented by the aliphatic alcohols and acids containing hydrocarbon radicals with 23 C atoms; as far as we know, such compounds are important for the synthesis of antitubercular and antileprous agents [3] and were formerly difficultly accessible.



For the purpose of quantitative determination of β-sitosterol we utilized its behavior with bromine. Bromine adds on quantitatively at the double bond of ring B with formation of the 5,6-dibromo derivative:



Of the various methods of halogenation the best results were obtained by bromination of β-sitosterol with dibromopyridine sulfate in solution in glacial acetic acid (analogous to the determination of cholesterol [4])or by the bromide-bromate method [5].

EXPERIMENTAL

Crude Phytosterol

Crude phytosterol is a coarsely crystalline powder with a yellowish-grey color and a greasy luster. Addition of acetic anhydride and conc. sulfuric acid to is saturated chloroform solution brings about an intensification of color with passage through various tints from pink to blue-green. The bromine number is 21, the m.p. 80-130°; moisture content 5%; the proportion soluble in dichloroethane is 74%; the residue insoluble in dichloroethane amounts to 21%. The substance extracted with dichloroethane melts at 82-120°. Recrystallization from ethanol gives two fractions-sterols and aliphatic alcohols. Recrystallization from 18 times the amount of ethanol ensures the optimum conditions for resolution of the fractions, good filterability, and a relatively high degree of purity of the sterols. Repeated crystallization from 18 times the amount of ethanol makes possible the isolation of pure β-sitosterol with m.p. 134-136°.

Separation of β-Sitosterol from Crude Phytosterol

350 g crude phytosterol (corresponding to 370 g starting material), dried at 80°, was subjected to extraction in a Soxhlet apparatus with 1500 ml dichloroethane for 25-30 hours until a sample from the extractor just gave a very small precipitate (not more than 0.02 g from 1 ml dichloroethane extract withdrawn from the extractor with a pipet). At the end of the extraction the insoluble residue (salts of lignoceric acid) were separated, and the filtrate was conbined with the dichloroethane extract; the yield of dry residue insoluble in dichloroethane amounted to 77-78 g (21% on the crude phytosterol). Distillation of the dichloroethane, at first at the ordinary pressure and towards the end at 100 mm, gave 272 g substance (77.7%) which was dissolved in 5 liters ethanol with refluxing and stirring. At 38-40° the solution was filtered through a heated porcelain funnel. The sterols collected on the filter were dried at 60-65°; yield 96 g (35% on the dry dichloroethane extract), m.p. 133-136°.

On cooling, the filtrate deposited the aliphatic alcohols contaminated with sterols; separation yielded 125 g dry substances melting at 67-100°.

96 g sterols were crystallized from 1700 ml ethanol to give 85 g of a substance with m.p. 134-136°. A mixed test with the β-sitosterol isolated from β-sitosterol benzoate [1] did not show a depression; $[\alpha]_D - 35°$ (in chloroform); bromine number 37-39; calc. 38.57.

The mother liquor after the second ethanolic crystallization (d 0.82) was used for crystallization of the aliphatic alcohols; at 40° 23 g sterols were separated with m.p. 126-131°. This was added to the sterols fraction which was subjected to a second crystallization from ethanol; in this way the yield of sterols (β-sitosterol) was raised to 29-30%.

The precipitate which came down on cooling the mother liquor was collected and dried at 50°; yield 94 g aliphatic alcohols with m.p. 66-68° (25% on the crude phytosterol). After driving off the ethanol from the mother liquor, there was left 18-20% of solids with m.p. 80-90° and consisting of a mixture of aliphatic alcohols and sterols.

Quantitative determination of β-sitosterol

a) Determination of β-sitosterol with the help of dibromopyridine sulfate. 0.2-0.3 g exactly weighed β-sitosterol (dried at 100°) is placed in a flask with a ground glass stopper and dissolved in 15-20 ml chloroform; to the solution is added 15-20 ml of a solution of dibromopyridine sulfate. After 5 minutes' shaking, the contents of the flask should be transparent and yellow in color. In the event of turbidity a few milliliters of glacial acetic acid should be added until the solution clears (the excess of halogen amounts to 25-30% of the theoretically required amount). Back-titration is carried out with 0.1 N sodium thiosulfate solution after addition of 15 ml 10% potassium iodide solution, 50 ml water and 5 ml 0.5% starch solution (a blank is run in parallel).

Calculation is performed with the formula:

$$X = \frac{(a-b) \cdot 0.007992 \cdot 100}{c},$$

where X is the bromine number, a is the number of milliliters of 0.1 N dibromopyridine sulfate solution, b is the number of milliliters of 0.1 N sodium thiosulfate solution, and c is the weight of substance in grams.

The solution of dibromopyridine sulfate is prepared as follows: 8 g pyridine and 10 g sulfuric acid (d 1.84) were dissolved separately, each in 20 ml glacial acetic acid, and to the mixture was added 8 g bromine dissolved in 20 ml glacial acetic acid; the final solution was made up to 1 liter with glacial acetic acid.

The method for quantitative determination of β-sitosterol was tested on samples prepared by saponification of β-sitosterol-3-benzoate and twice recrystallized from ethanol. The date obtained are set forth in Table 1.

TABLE 1

Determination of Bromine Number of β-Sitosterol with the help of Dibromopyridine Sulfate

c	a − b	X
0.1470	7.10	38.6
0.2210	10.70	38.6
0.1438	7.02	38.8
0.2594	12.48	38.5

TABLE 2

Determination of Bromine Number of β-Sitosterol by the Bromide-Bromate Method

c	a − b	X
0.4190	19.99	38.13
0.3998	19.18	38.32
0.4668	22.48	38.49
0.3744	18.11	38.57

b) Determination of β-sitosterol by the bromide-bromate method. 0.3-0.5 g β-sitosterol (exactly weighed and dried at 100°) is placed in a flask with a ground-glass stopper; it is dissolved in 15 ml chloroform and addition is made of 25-35 ml 0.1 N potassium bromate solution, 10 ml 10% HCl and 1 g potassium bromide. After 15-20 minutes, addition is made of 20 ml 10% potassium iodide solution; the liberated iodine is titrated with 0.1 N sodium thiosulfate solution in presence of 5 ml 0.5% starch solution. A blank is run at the same time. Reaction temperature 6-9°.

In Table 2 are set forth the results of analysis of β-sitosterol prepared by saponification of β-sitosterol 3-benzoate.

The date of Tables 1 and 2 show that the results are perfectly satisfactory. (Thecalculated theoretical bromine number of β-sitosterol is 38.57.)

SUMMARY

1. A method is developed for the separation of β-sitosterol from vegetable sterols (phytosterol) based on extraction of the sterols with dichloroethane and recrystallization from ethanol.

2. It is shown that β-sitosterol can be quantitatively determined with the help of dibromopyridine sulfate (dissolved in glacial acetic acid) or of the bromide-bromate method.

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THE STRUCTURE OF SULFONIC ACIDS OF 2-AMINO-4-METHYLTHIAZOLE

II. CLARIFICATION OF THE STRUCTURE OF THE SULFONIC ACIDS OF 2-AMINO-4-METHYLTHIAZOLE WITH THE HELP OF INFRARED SPECTRA

S.G. Bogomolov, Yu.N. Sheinker and I.Ya. Postovsky

Depending on the reaction conditions the sulfonation of 2-amino-4-methylthiazole [1] may yield two isomeric sulfonic acids: a low-melting l (m.p. 256°) and a high-melting one (m.p. 360° with decomp.), the low-melting isomer changing into the other when heated with sulfuric acid.

The problem of the structure of these acids and their respective derivatives had been a debatable one until recently. In most papers [2-4] the authors arrived at the conclusion that the low-melting acid is the sulfamic acid of 2-amino-4-methylthiazole and the high-melting acid is 2-amino-4-methylthiazole-5-sulfonic acid.

In the preceding paper [5] fresh chemical facts were submitted which refuted the above conclusion. The new data indicated that the low-melting acid is the sulfonic acid (the product of chlorosulfonation of 2-acetylamino-4-methylthiazole is the N-acetylated chloride of this acid), while the high-melting acid is evidently the sulfamic acid. In the light of these conclusions the transition of the low-melting into the high-melting acid is a rearrangement of sulfonic acid into sulfamic acid, and represents the first observed case of a transition of this type, which is opposite in character to analogous transformations in the series of aniline derivatives. For this reason, we considered it necessary to obtain supplementary evidence of the structure of these compounds, using not chemical, but physical methods, and particularly the method of infrared spectroscopy. On the basis of a study of the infrared absorption spectra of the isomeric sulfonic acids of 2-amino-4-methylthiazole and of a series of other derivatives of 2-aminothiazole, we have now obtained confirmation of the conclusions reached in the preceding paper [5].

EXPERIMENTAL

The infrared spectra of the 16 compounds listed in the table were plotted. For some of the compounds in the table the position of some substituted groups or atoms in the molecules is not indicated since their position was the subject of the present research.

All the substances were first repeatedly recrystallized until their melting points were constant.

Infrared absorption spectra in the 2 to 12.5 μ region were plotted with the help of an ISP 14^{b} infrared spectrometer with a NaCl prism. The apparatus was equipped with a simple mechanism permitting practically simultaneous regulation of the position of the zero point on the photogram, the transmissibility of air and the transmissibility of the sample of the investigated substance. For compensation of the drop in intensity of the source of radiation (carborundum rod) the width of the inlet and outlet slits during operation was automatically increased from 0.1 to 1 mm.

In addition to the apparatus with NaCl prism, the 2 to 3.5 μ region was measured with a spectrometer equipped with a LiF prism* which has a greater dispersion in this region.

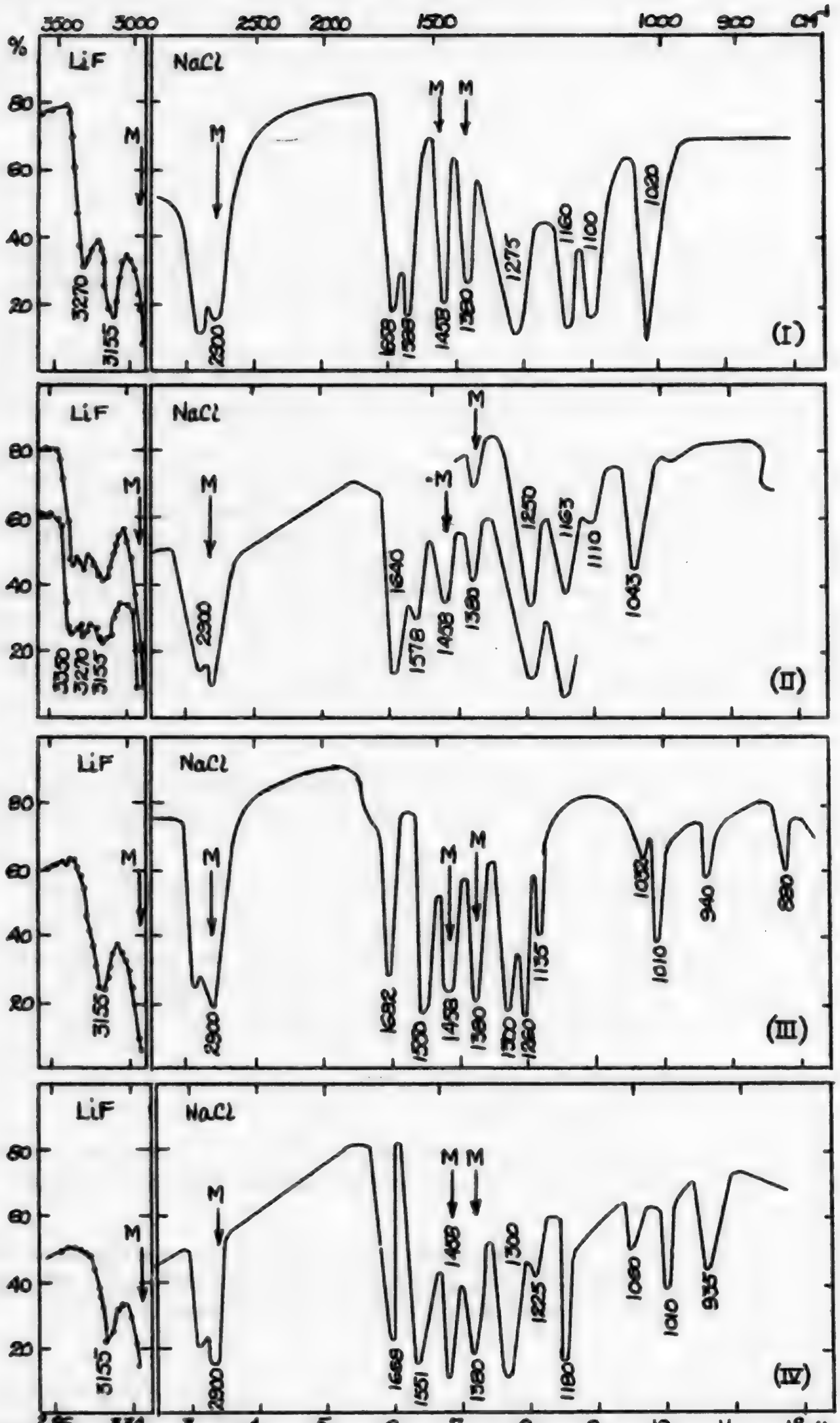
Since nearly all of the investigated substances were distinguished by extremely poor solubility in solvents applicable for infra red spectroscopic work, the substances were investigated in the solid crystalline form in suspension in petroleum jelly.

The absorption spectra of all the investigated substances are represented in the diagrams on which the abscissas are wave-lengths in μ (or wave number in cm^{-1}) and the ordinates are percentage transmissions. Absorption bands originating from the petroleum jelly are indicated in the diagrams by letter M.

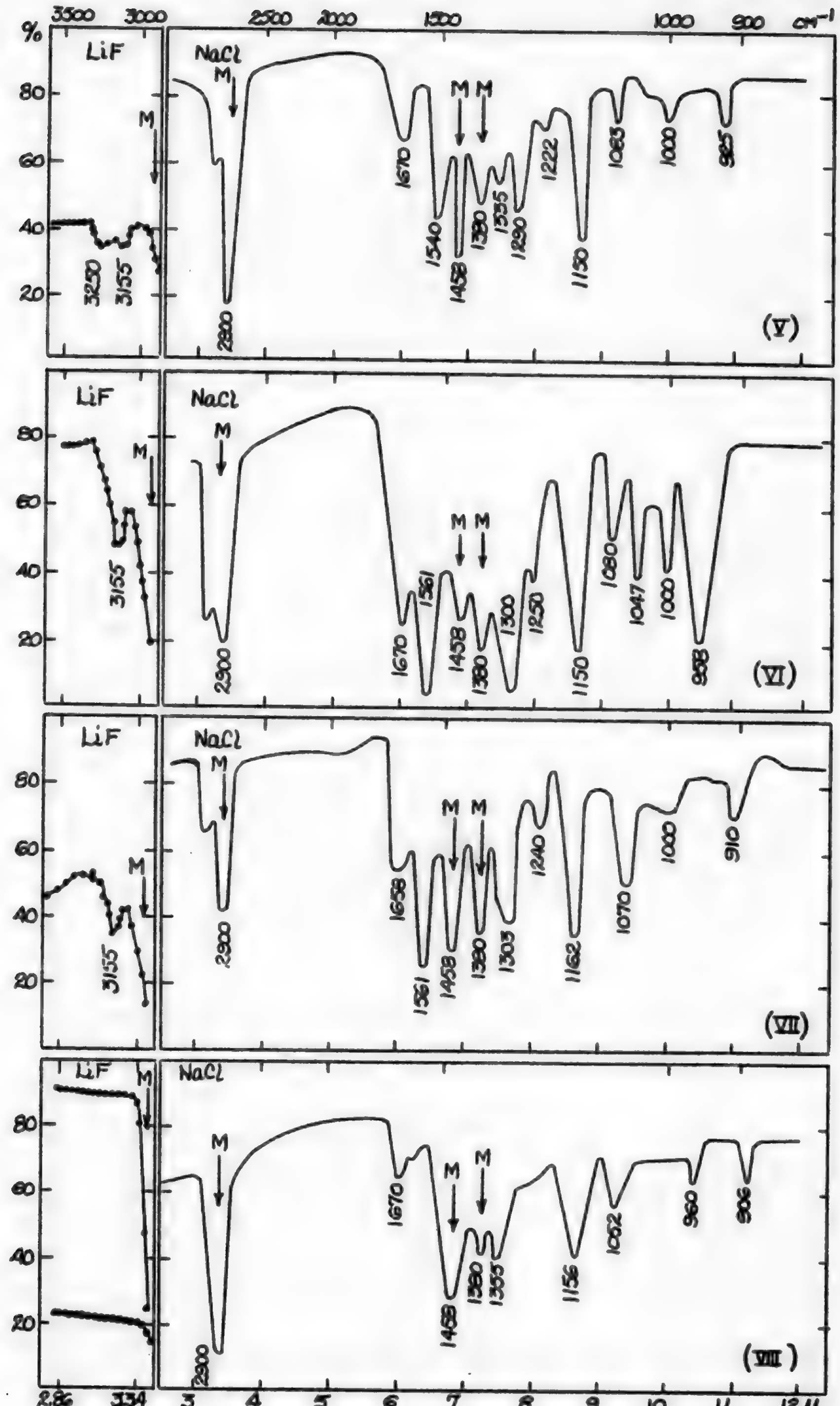
Evaluation of Results

The solution in this investigation of the problem of the structure of the sulfonic acids of 2-amino-4-methylthiazole and some of their derivatives is founded on consideration of the data for absorption by these compounds of radiation in the spectral region of 3000-3700 cm^{-1} (3.3-2.6 μ). This region contains characteristic absorption bands of the NH groups (likewise OH); depending upon the nature of these groups (e.g. whether NH or NH_2)

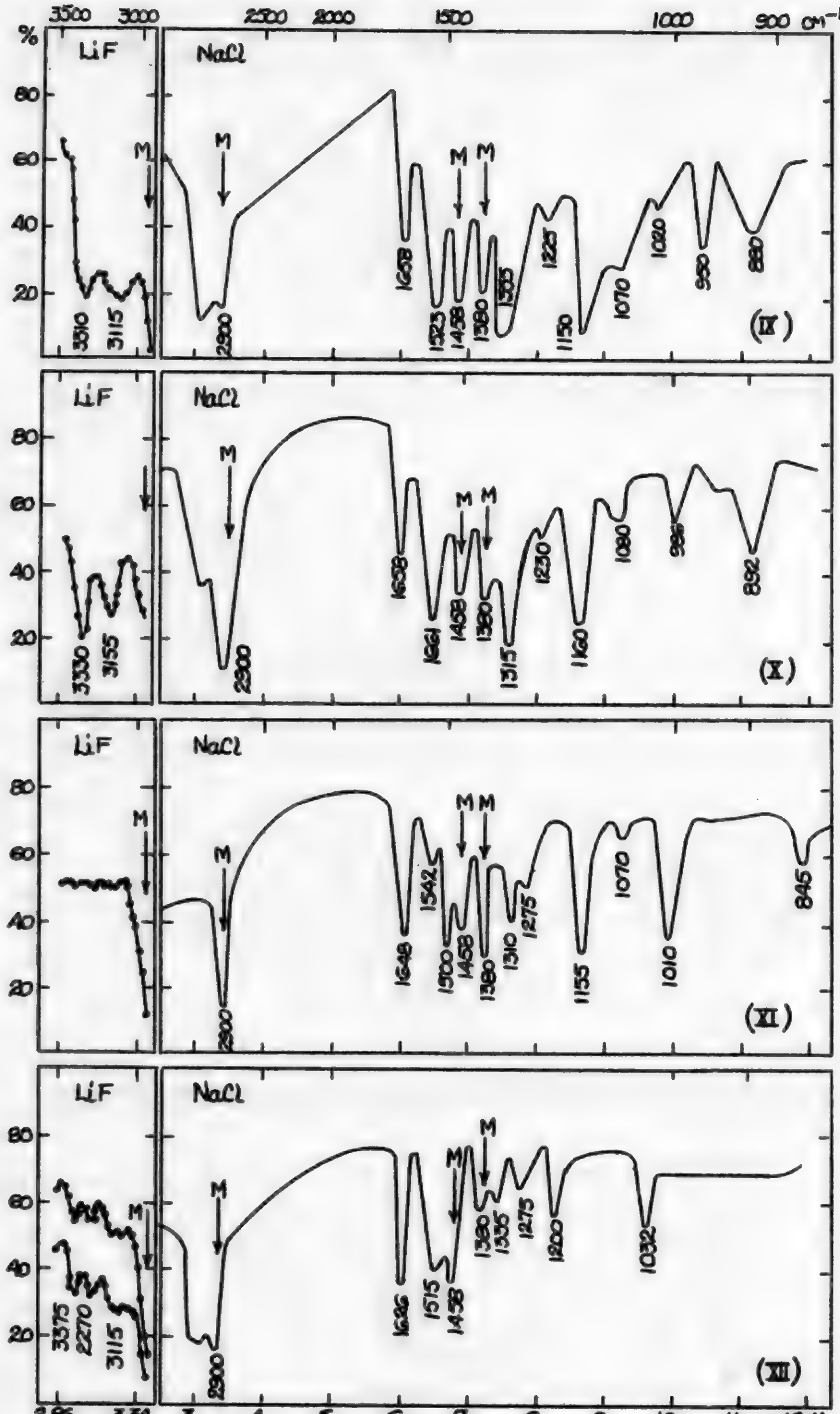
* The possibility of effecting measurements with an apparatus containing a LiF prism was kindly suggested to us by D.N. Shigorin, to whom the authors convey their thanks.



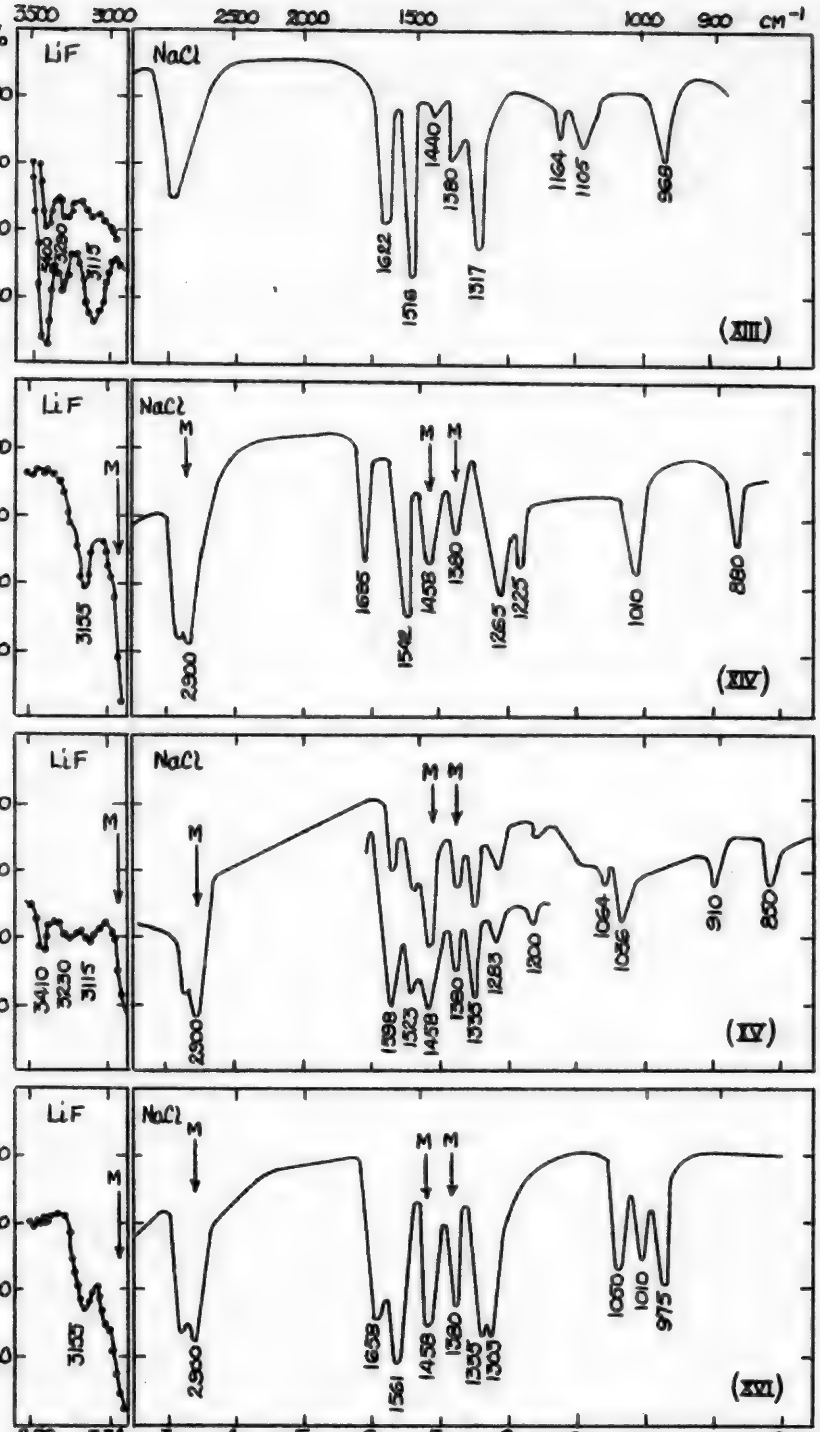
%
LiF
NaCl
M
(I)
(II)
(III)
(IV)



%
3500
3000
2500
2000
1500
1000
900
CM-1
LiF
NaCl
M
3250
3155
2900
1670
1540
1458
1380
1335
1290
1222
1150
1063
1000
925
(V)
3155
2900
1670
1561
1458
1380
1300
1250
1150
1080
1047
1000
958
(VI)
3155
2900
1658
1561
1458
1380
1303
1240
1162
1070
1000
910
(VII)
2900
1670
1458
1380
1355
1156
1052
960
906
(VIII)
80
60
40
20
2.86
3.34
3
4
5
6
7
8
9
10
11
12 μ



3500 3000 2500 2000 1500 1000 900 cm⁻¹
%
LiF
NaCl
M
(IX)
(X)
(XI)
(XII)
2.86 3.34 3 4 5 6 7 8 9 10 11 12 μ



3500
3000
2500
2000
1500
1000
900
CM-1
%
LiF
NaCl
1622
1516
1440
1380
1317
1164
1105
968
3410
3280
3115
(XIII)
M
3155
2900
1635
1542
1458
1380
1265
1225
1010
880
(XIV)
3410
3230
3115
1598
1523
1458
1380
1335
1283
1200
1064
1036
910
850
(XV)
3155
1658
1561
1458
1380
1335
1303
1050
1010
975
(XVI)
2.86
3.34
3
4
5
6
7
8
9
10
11
12 μ

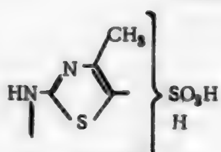
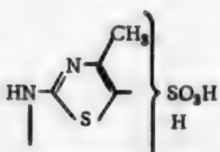
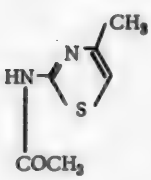
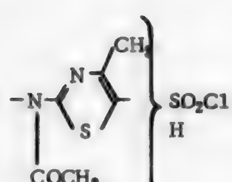
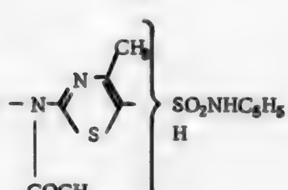
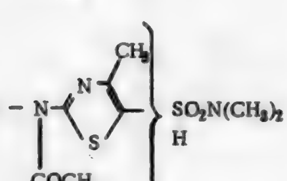
the system of characteristic bands in general will vary.

Complete absence of bands in this region is naturally due to the absence of such groups from the investigated molecules.

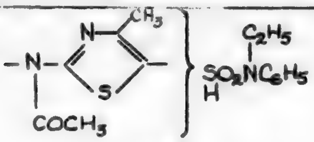
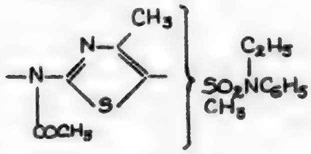
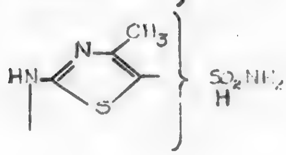
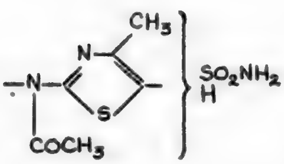
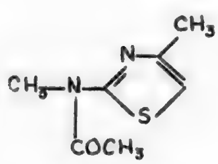
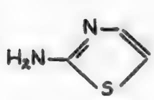
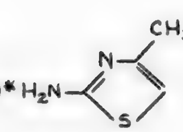
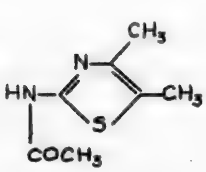
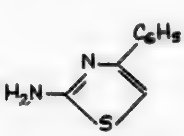
We applied these considerations to the evaluation of the experimental data.

It was found expedient to carry out this evaluation in such a manner that the data obtained for compounds of doubtful structure should be comparable with data for compounds of known structure; a series of compounds were therefore included in the investigation which did not belong directly to the same narrow group of 2-aminothiazole derivatives whose structure it was necessary to establish.

The position of the absorption bands in the spectra of all the investigated compounds in the 3000-3700 cm^{-1} region is set forth in the table.

Compound	Melting point (in °C)	Position of minima of bands in 3000-3700 cm^{-1} region			
(I)  Low-melting acid	256		3270		3115
(II)  High-melting acid	360 (with decomp.)	3350	3270	3155	
(III) 	132			3155	
(IV) 	159–160			3155	
(V) 	197–198		3250	3150	
(VI) 	242–243			3155	

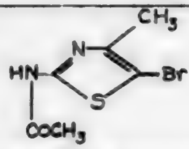
(Continued on following page)

Compound	Melting point (in °C)	Position of minima of bands in 3000-3700 cm⁻¹ region			
(VII) 	188-189			3155	
(VIII) 	128-129	No absorption			
(IX) 	168-169	3310			3115
(X) 	225-226	3330		3155	
(XI) 	110	No absorption			
(XII) 	89	3375	3270		3115
(XIII)* 	42	3400	3290		3115
(XIV) 	146-147			3155	
(XV) 	149	3410	3230		3115

(Continue on following page)

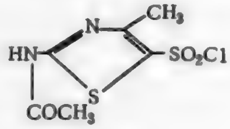
* The compound was investigated in the fused state.

(Continued)

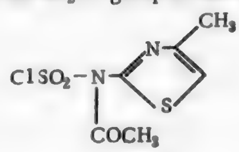
Compound	Melting point (in °)	Position of minima of bands in 3000-3700 cm^{-1} region				
	206				3155	

We see from the table that in the spectra of compounds (III), (XIV) and (XVI), in which the presence of one NH group is authenticated (the structure of these compounds was previously established with reasonable certainty [6,7], an absorption band in the 3155 cm^{-1} region is plainly visible. This band undoubtedly relates to vibration of the NH group since there are no other groups present which could possess absorption bands in this region. The considerable displacement of the band of the NH group in the direction of lower frequencies in comparison with the position of the band of the free NH group (3300 to 3400 cm^{-1}) testifies to the presence of strong intermolecular interaction in these compounds in the crystalline state.

In the spectrum of the product of sulfochlorination of 2-amino-4-methylthiazole (IV) we also find in this region an absorption band with a minimum at 3155 cm^{-1}. Consequently this compound contains an NH group and has the structure corresponding to formula (IVa), i.e. it contains the SO_2Cl group in the 5-position.



(IVa)



(IVb)

If the SO_2Cl group were present in this compound at the acetylated nitrogen atom and if the compound had the structure (IVb), then the band corresponding to the NH group should not be observable in the spectrum. Actually an absorption band is not observed in the spectra of compounds (VIII) and (XI) in which all the hydrogen atoms at the amino nitrogen are substituted (see the respective spectra).

Since the starting substance for the remaining investigated compounds containing the $SO_2NR_1R_2$ group is substance (IV), it may be thought that they all possess a similar structure, i.e. that they contain the $SO_2NR_1R_2$ group in the 5-position (R_1R_2 =H, Alk, Ar). The spectra of these compounds confirm this supposition. Thus the spectra of (V), (VI), (VII) and (X) have an absorption band in the 3155 cm^{-1} region corresponding to the NH group.

In the spectra of compounds (V) and (X) the presence in the $SO_2NR_1R_2$ radical of NH and NH_2 groups leads to the appearance in the 3000 to 3700 cm^{-1} region of supplementary absorption bands corresponding to these groups. In all these compounds, therefore, an NH group is present (at the amino nitrogen) and the $SO_2NR_1R_2$ is located in the 5-position.

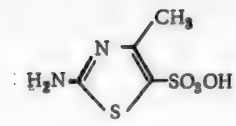
Substance (IV) (2-acetylamino-4-methylthiazole-5-sulfochloride) may be the starting substance for preparation of the low-melting sulfonic acid (I) which is formed from it by hydrolysis. Consequently the sulfo group in this compound must likewise be in the 5-position, while 2 hydrogens are linked to the amino nitrogen

For the purpose of obtaining spectral confirmation of this hypothesis we first found it necessary to examine the spectra of compounds in which an NH_2 group was present in the 2-position of the thiazole ring.

This was necessary because in all the compounds hitherto considered not more than one hydrogen atom was present at the nitrogen in the 2-position. At the same time the sulfonic acid (if the above supposition is correct) must contain a NH_2 group whose absorption bands must differ from the absorption bands of the NH group.

Spectra of the compounds (XII), (XIII) and (XV) were plotted, and their examination shows that the NH_2 group in the 2-position of the thiazole ring (in the crystalline state) is represented in the spectra by a stable band at 3115 cm^{-1} and by two less stable bands at 3270 and 3400 cm^{-1}.

On comparing the spectra of these compounds with the spectrum of the low-melting sulfonic acid, we can see that the latter also contains absorption bands in the region of 3115 and 3270 cm^{-1}. Hence it follows that this compound contains a NH_2 group (and no NH which is characterized by a band at 3155 cm^{-1}) and that the structure of the low-melting acid corresponds to formula (Ia). Consequently the low-melting acid is 2-amino-4-methylthiazole-5-sulfonic acid, as also follows from the chemical data [5].



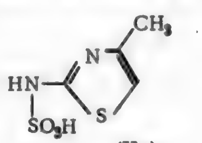
(Ia)

It is noteworthy that the spectrum of this compound is deficient in a third band, which is characteristic of the above-considered compounds containing NH_2 groups (3400 cm^{-1}), as well as in absorption bands in the 3300 to 3700 cm^{-1} region which should be assigned to vibrations of the OH group. It may be suggested that this is due to intermolecular interaction of the OH and NH groups which shifts the corresponding bands into the region of other observed bands (3300 to3100 cm^{-1}).

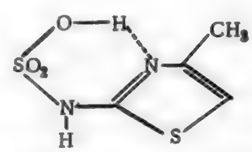
A similar spectrum is exhibited by compound (IX), prepared from (IV) by the action of ammonia. Due to the synthesis conditions, the SO_2NH_2 group must be in the 5-position and the NH_2 group in the 2-position, as in compound (I). In the spectrum of this compound (IX) are two bands at 3115 and 3300 cm^{-1} (as in the spectrum of the acid).

The high-melting sulfonic acid (II), obtained from the low-melting acid by heating with sulfuric acid, contains in its spectrum an absorption band at 3155 cm^{-1} as well as bands at 3270 and 3350 cm^{-1}. The 3155 cm^{-1} band, as noted above, is characteristic of the NH group in the compounds in question. Consequently this compound contains an NH group and has structure (IIa), i.e. it is 4-methylthiazole-2-sulfamic acid.

The remaining two absorption bands of this compound in the region considered are, in our opinion, associated with vibrations of the OH group which must participate both in intermolecular and intramolecular interaction. In the latter case the formation is extremely probable of an intramolecular hydrogen bond between the oxygen of the hydroxyl group and the nitrogen of the thiazole ring in the 3-position (IIb).



(IIa)



(IIb)

Examining the spectra in the region of lower frequencies, we may note that all the compounds exhibit two intense absorption bands at approximately 1550 to 1650 cm^{-1} which, judging by the literature data [8], are characteristic of the thiazole ring. Evidently in a series of compounds there is superposition of the above-noted bands on the absorption bands associated with the CO group of the acetyl radical or with deformed vibrations of the NH_2 group.

An intense absorption band in the 1150-1160 cm^{-1} region is observed for compounds whose molecules contain an SO_2 group. This absorption band evidently relates to the symmetrical vibration of the SO_2 group. According to the literature [9] this vibration has a value of 1150 cm^{-1} in sulfones.

SUMMARY

Consideration of the infrared spectra of the investigated compounds leads to the following conclusions.

1. The low-melting acid obtained by sulfonation of 2-amino-4-methylthiazole is 2-amino-4-methylthiazole-5-sulfonic acid (Ia), and the isomeric high-melting acid, formed from the low-melting acid by heating with H_2SO_4, is 4-methylthiazole-2-sulfamic acid (IIa).

2. The product of chlorosulfonation of 2-acetamino-4-methylthiazole is the N-acetylated acid chloride of the 5-sulfonic acid, and all the sulfamides obtained from the acid chloride are amides of this acid.

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* See Consultants Bureau Translation, p. 1863.

MECHANISM OF HETEROGENEOUS CATALYTIC ISOMERIZATION OF HYDROCARBONS OVER ACIDIC CATALYSTS

I. MECHANISM OF INTERACTION OF PINENE, CAMPHENE AND LIMONENE WITH ISOMERIZATION CATALYSTS —TITANIUM DIOXIDE AND ACTIVATED CLAY

G. A. Rudakov, Z. S. Khomenko and M. M. Shestaeva

The catalytic isomerization of pinene over activated clays, discovered by Gurvich [1], has been studied by Tishchenko and Rudakov [2] who reached the conclusion that this catalyst behaves like an acid during the reaction. They based their conclusion both on the evidence in the literature about the acidic nature of clays [3, 4] and on the nature of the products which were obtained from pinene under the action of certain acids [5, 6].

The enunciated ideas about the role of the catalyst in the reaction were later widely accepted and were applied both to other hydrocarbons and other catalysts. Concerning, however, the mechanism of reaction of the liquid hydrocarbon with the solid catalyst, it has remained unclarified.

Tishchenko and Rudakov suggested that during the catalytic isomerization of pinene over activated clays, formation takes place, at the surface of the colloidal particles of aluminosilicic acids entering into the composition of clays, of unstable ethers which are susceptible to a series of rearrangements and whose breakdown results in products of isomerization of pinene — camphene and limonene.

During the past 20 years the ideas in question have undergone some modification, and recently a theory of the mechanism of isomerization of hydrocarbons over aluminosilicate and similar catalysts which has gained wide currency is based upon transformations of unstable carbonium ions which are formed by detachment of a proton from the catalyst and its addition to the unsaturated hydrocarbon [7, 8, 9]. An electron deficiency round one of the carbon atoms of the carbomium ion (sextet) is, according to this theory, the cause of the readily occurring rearrangement of the ion. Return of the proton to the catalyst or its transfer to another molecule of hydrocarbon after rearrangement of the cation leads to formation of a new isomer. A series of facts support the views enunciated about the mechanism of the reaction. These include the observations of Meerwein and coworkers [6, 10] on the ionic character of the retropinacoline rearrangement of the ether of isoborneol into the ether of camphene hydrate in a homogeneous medium, and the greater ease of understanding of the many processes from the standpoint of transformations of the carbonium ion. Unfortunately, the ionic concepts of the mechanism of heterogeneous isomerization of liquid hydrocarbons on acidic catalysts of the aluminosilicate type have been little developed, so that their value has been considerably reduced. While explaining some phenomena, these concepts lead to a series of problems which are not answered by the authors who have advanced the ionic mechanism of the reaction. Still unclarified is the state of the carbonium ions: are they, to any extent, free, like ions in solution, or are they all fixed to the surface of the catalyst, retaining on this surface the negative charges of the lattice as in the case of Ag^+ ions attached to the surface of AgCl particles? The assumption without special reservations of transfer of a protonfrom a carbonium ion to a hydrocarbon molecule with transformation of the latter into a new ion should, namely, lead to the assumption of the possibility of transfer of a proton from the surface to the space since the carbonium ion located at the surface of the catalyst is surrounded not only by molecules directly bordering on this surface. But if we assume the transfer of a proton into the space, we must also assume the presence during the reaction of a certain, if small, number of free ions in solution, and consequently we would be compelled to assume also the occurrence of a reaction outside the catalyst surface. In that event, the reaction, while starting at the catalyst surface, would continue in the course of a chain process outside this surface until the proton had been returned to the catalyst. The charge formed at the surface of the catalyst may, however, also be neutralized by other processes, for example the transfer of a proton to the catalyst by a molecule of hydrocarbon with simultaneous transformation into a carbonium ion. If transfer of a proton from the surface to the space is impossible, due for example to orientation of the carbonium ion by its positive charges toward the negative charges of the lattice, then proton transfer from the carbonium ion to the molecule bordering upon this ion at the catalyst surface must be of limited occurrence since the carbonium ion will be capable of transferring its proton only to that molecule which occupies the same position in relation to the anion of the lattice which it occupies itself.

The foregoing explanation of the mechanism of the reaction is extremely close to the explanantion given

by Tishchenko and Rudakov. In both cases the formation is suggested at the catalyst surface of an intermediate compound — an ether; in both cases this intermediate compound is assumed to undergo rearrangement. But if we assert that the reaction involves rearrangement of the carbonium ion, this intermediate compound must be considered to be ionized. The concept of the ion in this explanation of the mechanism is similar to the concept of the ion in the crystal lattice or to the concept of the ion adsorbed by the lattice.

The investigations described below of the catalytic transformations of pinene, camphene and limonene on titanium dioxide and activated clay permit us to reach conclusions as to whether the reaction only proceeds at the catalyst surface or whether it is transferred to the space, while not touching upon the question of the ionic or non-ionic character of the reaction. Terpenes proved to be exceptionally convenient starting materials for this purpose since the lability of terpenes enabled the reaction to be conducted at relatively low temperature so that the reaction was not complicated by thermal transformations; moreover, as will be seen later, observations of isomeric transformations could be very conveniently made on the basis of changes of optical activity during the reaction.

As we know, the heating of α-pinene with active clays [2,11], titanium dioxide [12,13] and many other similarly acting catalysts results in its isomerization with formation of camphene, tricyclene, bornylene, fenchenes, limonene (dipentene), terpinolene and terpinenes. The main products of the reaction are camphene and monocyclic terpenes.

Isomerizing transformations of α-pinene are accompanied by changes of optical activity: the optical rotation of the mixture of reacting substances, i.e. a mixture of pinene and its transformation products rises during the first phase of the reaction, reaches a maximum before complete isomerization of the pinene, and then falls off rapidly (Figs. 1 and 1a).

The optical rotation of the reaction mixture rises at the start of the reaction because the α_D of the formed camphene and limonene is considerably higher than the α_D of the original pinene. The fall in optical rotation of the reaction mixture at the close of the reaction is due to various causes: in the reaction conditions the limonene may be transformed into terpinolene and terpinenes; also, as was established in the present investigation, the limonene may racemize; camphene also racemizes when heated with a catalyst due to reverse transformation into tricyclene [13] and possibly also to simultaneous rearrangement of the second order [14] which, as shown in the present investigation, may proceed with exceptional speed.

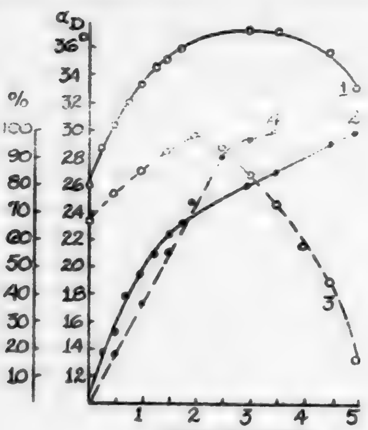

Fig. 1. Change of α_D of reaction mixture of terpenes during isomerization of pinene; 1) α_D of isomerizate obtained from pinene (sample 1, Table 1) when heated with 0.1% titanium dioxide at 60°; 2) % transformation of pinene (sample 1, Table 1) on heating with 0.1% titanium dioxide at 160°; 3) α_D of isomerizate obtained from pinene (sample 2, Table 1) on heating with 1% activated clay at 125°; 4) % transformation of pinene (sample 2, Table 1) when heated with 1% activated clay at 125°.

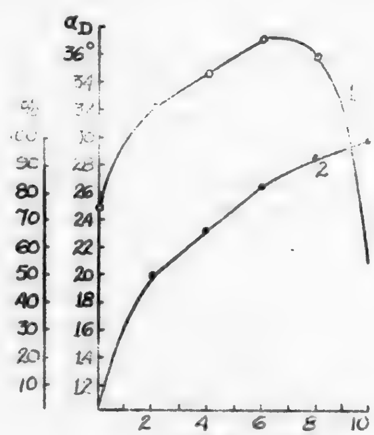

Fig. 1a. Change of α_D of reaction mixture of pinenes during isomerization of pinene

1) α_D of isomerizate obtained from pinene (sample 3, Table 1) on heating with 0.5% titanium dioxide at 135°; 2) % transformation of pinene.

It might be thought that the formation of camphene and limonene from pinene and their racemization proceed simutaneously and independently of one another. The rise of optical rotation during the first phase could then be regarded as the result of more rapid accumulation of products of

of pinene), while the fall of optical rotation during the second phase may be regarded as the result of more rapid racemization of the products of reaction, coupled with their increasing concentration and the fall of concentration of pinene.

Careful analysis of the phenomenon compelled us to reject the foregoing hypothesis. On the basis of measurements of the α_D of the reaction mixture comprising pinene and the products of its isomerization obtained at different intervals during the reaction, and from determinations of the pinene content in this mixture effected at the instant of measurement of the α_D, it was possible to calculate the α_D of the mixture of substances formed from pinene at different instants of the reaction. It was found that the α_D of the products of isomerization remains constant as long as pinene is present in the reaction mixture in concentration not below 25-35%; only subsequently does rapid racemization of these products supervene (Figs. 2 and 3).

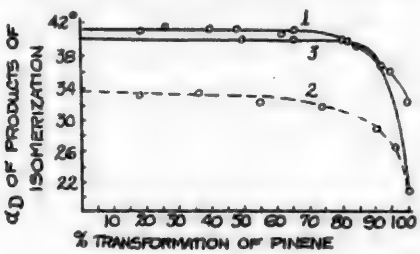

Fig.2. Change of α_D of products of isomerization as a function of the percentage transformation of pinene. 1) α_D of products of isomerization obtained from pinene (sample 1, Table 1) on heating with 0.1% titanium dioxide at 160°; 2) α_D of products of isomerization obtained from pinene (sample 2, Table 1) on heating with 1% activated clay at 125°; 3) α_D of products of isomerization obtained from pinene (sample 3, Table 1) on heating with 0.5% titanium dioxide at 135°.

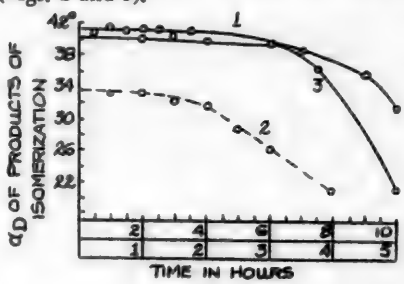

Fig.3. Change of α_D of products of isomerization of pinene as a function of the duration of the reaction.

1) α_D of products of isomerization obtained from pinene (sample 1, Table 1) on heating with 0.1 % titanium dioxide at 160°; 2) α_D of products of isomerization obtained from pinene (sample 2, Table 1) on heating with 1% activated clay at 125°; 3) α_D of products of isomerization obtained from pinene (sample 3, Table 1) on heating with 0.5% titanium dioxide at 135°.
For 1 and 2 the duration is plotted on the lower scale; for 3 it is plotted on the upper scale.

The results obtained led to the conclusion that the catalyst begins to act upon the products of isomerization of pinene only after the main bulk of the pinene has reacted. In order to verify this conclusion experiments were carried out during which optically active camphene and limonene, dissolved in optically inactive pinene, were heated with titanium dioxide. The results of these experiments, plotted in Figs. 4 to 7, fully confirm this conclusion: both camphene and limonene, when dissolved in racemic pinene, retain their optical rotation when heated with the catalyst as long as the pinene concentration does not drop below a certain level. Inspection of the curves of change of α_D as a function of the duration of reaction (Figs. 3, 5 and 7) indicates that the activity of the catalyst gradually falls off during the reaction due to poisoning; therefore, the drop in α_D at the end of the reaction is less steep than it would have been if the catalyst had retained constant activity. A noteworthy feature is a certain difference between the behavior of optically active camphene and limonene, dissolved in racemic pinene, when heated with titanium dioxide at 160°. The start of racemization of limonene occurs at a concentration of residual pinene in the solution of about 30%, and racemization subsequently proceeds fairly quickly. Racemization of camphene on the other hand starts at a concentration of the residual pinene of about 50% but proceeds slowly in contrast to the extremely rapid racemization of pure camphene when heated with the same catalyst (Fig.5). It is interesting that camphene formed in the process of isomerization of pinene by titanium dioxide starts to racemize later, at a concentration of pinene in the reaction mixture of about 30% (Fig.2). From these data, obtained with two samples of camphene of different origins, we can conclude that racemization of camphene is retarded or even stopped because of the presence not only of pinene in the mixture but also of products of its isomerization, probably monocyclic terpenes or fenchenes. This is in agreement with existing data for the considerably stronger action of the catalyst upon fenchenes than upon camphene [11].

The very slight differences in behavior of camphene and limonene, dissolved in optically inactive pinene, when heated with titanium dioxide do not, however, alter the general picture of the process.

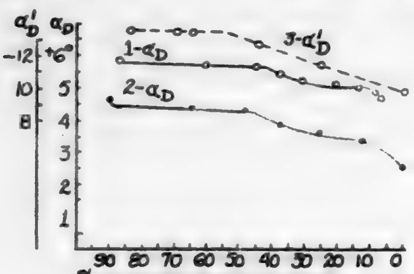

Fig.4. Change of α_D of solutions of camphene in racemic pinene on heating with titanium dioxide at 160° as a function of changes in their pinene content

1) α_D of 12.5% camphene solution (sample 2, Table 2) in pinene (sample 4, Table 1) on heating with 0.1% titanium dioxide; 2) α_D of 10% solution of camphene (sample 2, Table 2) in pinene (sample 4, Table 1) on heating with 0.15% titanium dioxide; 3) α_D of 16.2% solution of camphene (sample 1, Table 2) in pinene (sample 5, Table 1) on heating with 0.2% titanium dioxide added in two portions (0.1% at the start of the reaction and 0.1% at a concentration of the residual pinene of 65%).

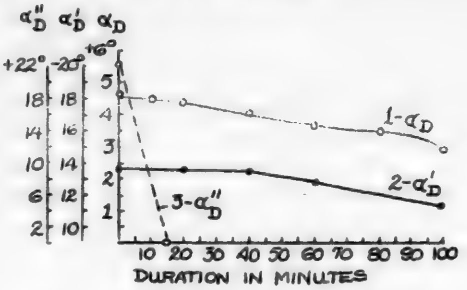

Fig.5. Changes of α_D of camphene on heating with titanium dioxide at 160° as a function of the duration of heating.

1) α_D of 10% camphene solution (sample 2, Table 2) in racemic pinene (sample 4, Table 1) on heating with 0.15% titanium dioxide; 2) α_D of 16.2% camphene solution (sample 1, Table 2) in racemic pinene (sample 5, Table 1) on heating with 0.2% titanium dioxide added in two installments (0.1% at the start of the reaction and 0.1% 40 minutes after the start of the reaction); 3) α_D of camphene (sample 3, Table 2) on heating with 0.1% titanium dioxide in absence of pinene.

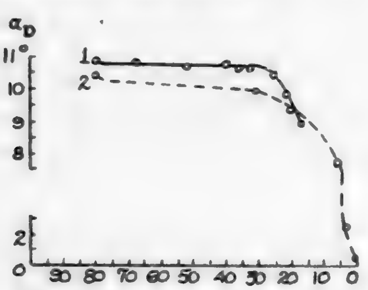

Fig.6. Change of α_D of a solution of limonene in racemic pinene on heating with titanium dioxide at 160° as a function of the changes of their pinene content.

1) α_D of 20% solution of limonene in pinene (sample 4, Table 1) on heating with 0.1% titanium dioxide; 2) the same with 0.2% titanium dioxide.

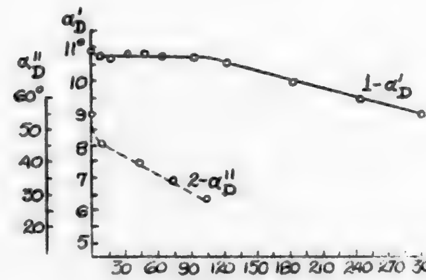

Fig.7. Changes of α_D of limonene in racemic pinene on heating with titanium dioxide at 160° as a function of the duration of heating.

1) α_D of solution of limonene in racemic pinene (sample 4, Table 1) on heating with 0.1% titanium dioxide; 2) α_D of limonene on heating with 0.1% titanium dioxide in absence of pinene.

The described course of the reaction is reliable evidence that the reaction takes place only at the surface of the catalyst. If the reaction had taken place in the space, it would have been difficult to explain why only a proton of a molecule of pinene should have been obtained in the space and not protons of the

molecules of limonene and camphene present in solution together with the pinene and which rapidly racemize in the absence of pinene. On the other hand, if we assume that the reaction proceeds only at the surface of the catalyst and that at the reaction temperature the pinene is selectively adsorbed on this surface, the described course of the reaction becomes perfectly intelligible.

EXPERIMENTAL

1. Starting materials

The catalysts — titanium dioxide and activated clay — used in the investigation were prepared by the usual methods [2,12]; in order to ensure results which would be as comparable as possible, the catalysts used were all prepared by one method.

Constants of the samples of pinene and camphene used in the investigation are set forth in Table 1.

TABLE 1

Data for Pinene Samples Used

No. of sample	Origin	α_D	n_D^{20}	d_4^{20}
1	from oil of turpentine	26.05°	1.4654	0.8580
2	" " " "	23.30	1.4654	0.8581
3	" " " "	24.90	1.4660	-
4	obtained by mixing d and l-pinene* (ex-turpentine)	0.02	1.4653	0.8578
5	obtained via the nitrosochloride [16]	0.46	1.4654	0.8572

TABLE 2

Data for the Samples of Camphene Used

No. of sample	Origin	Solidification temp. (in °)	$[\alpha]_D$ in benzene (c = 50%)	n_D^{54}	d_4^{54}	MR_D
1	from fir oil	46	−102.5°	1.4560	0.8398	44.09
2	obtained by isomerization of pinene	47.5	+55.5	1.4759	0.8508	44.03
3	obtained by isomerization of pinene	48	+22.3	1.4538	0.8437	43.70**

Limonene was isolated from the products of isomerization of pinene effected in presence of titanium dioxide as catalyst. Physical properties of limonene:

n_D^{20} 1.4729; d_4^{20} 0.8419; MR_D 45.35; calc. 45.24; α_D 54.78°; $[\alpha]_D$ 65°.

The individaul terpenes were isolated with the aid of the efficient rectifying columns previously described [15].

2. Isomerization of the terpenes

Isomerization of terpenes was carried out in a three-necked round-bottomed flask fitted with reflux condenser, thermometer and motor-driven stirrer. The amount of terpenes in individual experiments varied between 40 and 200 ml. In order to avoid poisoning of the catalyst by products of oxidation, the terpenes were used in the freshly distilled condition and 0.01% hydroquinone was added as inhibitor. The catalyst was added when a temperature 100° had been reached, and from the instant of attainment of a temperature 5° below the required one, the reckoning of duration and the periodic withdrawal of samples was started. The mixture was heated as rapidly as possible. In many cases the reaction temperature was governed by the boiling point of the mixture. In the case of isomerization of pinene, the mixture boiled at 155°, but due to the rapid accumulation of reaction products the boiling point quickly rose to 160°. Withdrawal of samples in the course of the process was effected with a pipet through the reflux condenser. The samples were filtered before determinations were carried out of their camphene content and α_D. The camphene content was determined by the formylation method

* We extend our best thanks to I. I. Bardyshev, who placed this sample at our disposal.

** Sample contains tricyclene as impurity.

[17] with introduction of a correction for incompleteness of the reaction (94%). Other terpenes which react with formic acid were analyzed by this method: tricyclene, bornylene and fenchenes. Employment for the polarimetric determinations of a tube 50 mm long and 2 mm in diameter in conjunction with the camphene determination enabled us to use samples of 2 g and even less.

3. Calculation of optical rotation of the products of isomerization

Unreacted pinene was also present in samples of isomerizate withdrawn in the course of the process and consisting mainly of camphene and limonene.

The additivity of the properties of solutions of terpenic hydrocarbons was taken into account in the calculation of the optical rotation of the products of isomerization contained in each sample, applying the following formula:

$$\frac{\alpha'_D \cdot n'}{100} + \frac{\alpha''_D \cdot n''}{100} = \alpha_D, \tag{1}$$

hence

$$\alpha''_D = \frac{100 \cdot \alpha_D}{n''} - \frac{\alpha'_D \cdot n'}{n''}, \tag{2}$$

where α_D is the optical rotation of the reaction mixture, α'_D is the optical rotation of the original pinene, α''_D is the required optical rotation of the products of isomerization, n' is the percentage of pinene in the reaction mixture, n'' is the percentage of products of isomerization in the reaction mixture. α_D and α'_D can be easily measured, while n' and n'' are mutually dependent since

$$n'' = 100 - n', \tag{3}$$

and hence for the calculation of α''_D it suffices to know n' or n". Since direct determination of n' or n'' consumes much time and a large amount of substance, determinations were made on the basis of indirect calculation from the readily determinable content of camphene in the samples (by the formylation method) according to the formula:

$$\frac{a}{b} \cdot 100 = n'', \tag{4}$$

where a is the percentage of camphene in the sample concerned, b is the percentage of camphene in the isomerizate at the instant of complete transformation of the pinene. Under the action of a mixture of HCOOH and H_2SO_4 in the reaction conditions, pinene is transformed to the extent of 10% on the average into an ether which results in too-high results for n'' when calculated according to formula (4) and correspondingly to too-low results for n'; a correction in accordance with formula (5) is, therefore, introduced into the values of n' calculated from formulas (3) and (4):

$$n'_{corr.} = n' + 0.099n' \cdot c^{-1} + 0.012n' \cdot c^{-2}, \tag{5}$$

where

$$c = \frac{b}{100}.$$

4. Establishment of racemization of limonene when heated with titanium dioxide

The starting product used in the investigation was an isomerizate with α_D 10.4°, n_D^{20} 1.4812, obtained from limonene by heating with 0.1% titanium dioxide for 3 hours; it contained 96% monoterpenes and 4% polymers. The monoterpenes (54 g) contained in the isomerizate, separated from polmers by vacuum-distillation of the isomerizate, were subjected to rectification, the results of which are plotted in Figure 8. The fractionation curves enable the fractions to be arranged in 5 groups denoted by the letters A to F.

Group A (2.8%, fraction 1 – n_D^{20} 1.4732; d_4^{20} 0.8504; α_D 8.72°) consists of an unidentified component present in admixture with monocyclic terpenes.

Group B (18.5%, fractions 2 to 8). The characteristic fraction of this group is fraction 6 (n_D^{20} 1.4768; d_4^{20} 0.8414; α_D 14.0°; b.p.173°). In the mixture of fractions of group B were found terpinene (nitrosite with m.p. 155°) and limonene which was isolated, after removal of α-terpinene, in the form of an adduct with maleic anhydride. For this purpose 1 g maleic anhydride was added to 5 g of the mixture of fractions in 5 ml anhydrous ether. After 48 hours the product was washed with 4% NaOH solution and after removal of the ether it was distilled in vacuum. The distilled limonene had the following constants: n_D^{20} 1.4749; d_D^{20} 0.8443; α_D 24.36°; tetrabromide of the dl-form, m.p. 125°.

Group C (15.5%, fractions 9 to 13) was regarded as an intermediate group and was not examined.

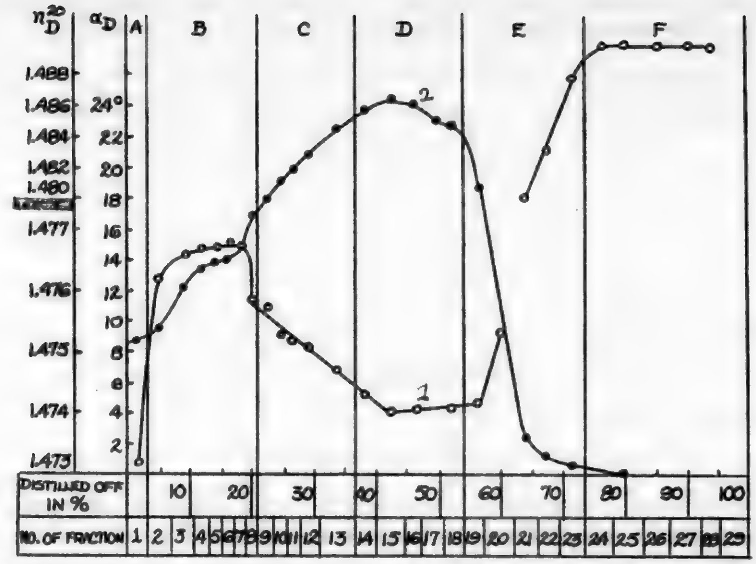

Fig.8. Results of rectification of products of isomerization of limonene.

1) n_D^{20}, 2) α_D.

Group D (17.4%, fractions 14 to 18) consists to a considerable extent of racemized limonene. All the fractions of this group were combined and treated with maleic anhydride. The limonene isolated after this treatment had the following constants which nearly coincided with those of the best 15th fraction: n_D^{20} 0.8436; α_D 24.8°; b.p. 175.5°; tetrabromide, m.p. 125°.

Group E (20.5%, fractions 19 to 23) may be regarded as intermediate between the limonene and terpinolene groups but apparently contains also γ-terpinene although we failed to obtain derivatives of the latter. Fraction 20, characteristic of Group E had the following properties: n_D^{20} 1.4759; d_4^{20} 0.8453; α_D 9.5°; b.p. 178°.

Group F (26.3%, fractions 24 to 29) consists mainly of terpinolene. The characteristic 26th fraction had the following constants: n_D^{20} 1.4906; d_4^{20} 0.8637; MR_D 45.7; calcd. 45.7, taking into account the hemicyclic position of the double bond; terabromide, m.p. 117°.

The foregoing data conclusively point to racemization of the limonene (fall in α_D from 54.78 to 24.8°).

Approximate composition of the isomerizate: limonene and dipentene 42, terpinolene 35, terpinenes 19, polymers 4%.

SUMMARY

1. Although pinene, camphene and limonene — separately — rapidly isomerize, while they also racemize when heated with titanium dioxide, camphene and limonene do not suffer any change when they are heated with the same catalyst in presence of pinene.

2. Catalytic isomerization of pinene over activated clay at 125° and over titanium dioxide at 135-160° leads to formation of camphene and limonene which resist the action of these catalysts until the pinene concentration in the reaction mixture falls to 25-35%.

3. The foregoing phenomena are due to reaction only taking place at the catalyst surface of the selectively adsorbed pinene and not in the liquid. This fact has general significance for the understanding of the mechanism of heterogeneous isomeric transformations of liquid hydrocarbons over catalysts like aluminosilicates and titanium dioxide.

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CONDENSATION OF PHENYLALUMINUM DIIODIDE WITH AROMATIC HALOGENATED DERIVATIVES

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Continuing our investigations into the reaction of phenylaluminum diiodide with halogenated derivatives [1,2], we have studied the condensation of $C_6H_5AlI_2$ with bromobenzene, p-chloro- and p-bromotoluenes. It was observed that with aliphatic iodides the facility of reaction depends markedly on the nature of the radical and the mobility of the halogen; it was, therefore, to be expected that condensations with aryl halides would only proceed in drastic conditions. In actual fact in the normal conditions of organometallic synthesis no reaction occurs: in these experiments yields of diphenyl of the order of 10-15% are due to its formation in the process of preparation of the organoaluminum compound.

Organoaluminum compounds are not exceptional in this respect. Phenyl derivatives of other, more active, metals – sodium, lithium and magnesium – in their reaction with halobenzenes [3] likewise give low yields of diphenyl (15-20%). Only in conditions facilitating the dissociation of C_6H_5Me into radicals is it possible to obtain yields of diphenyl close to the theoretical, for example in the condensation of phenylmagnesium bromide with bromobenzene in presence of $CoCl_2$ [4] or, as our investigations showed [1], by conducting the synthesis in an autoclave at 150-200°.

In the case of $C_6H_5AlI_2$ we succeeded in obtaining at 245-255° diphenyl in a yield of over 90% of the theoretical by interaction with bromobenzene and in a yield up to 30% with p-chlorotoluene (Tables 1 and 2). The aluminum halide formed during the reaction energetically reacts with the condensation product and easily resinifies it [5]; the reaction, therefore, calls for relatively short-period contact of the reactants (30-60 minutes) and strict maintenance of the specified temperature range; complete charring takes place at above 260° or on prolonged heating.

Products, apart from diphenyl, which could be isolated in condensations with bromobenzene were terphenyl, quaterphenyl and quinquephenyl. A crystalline substance with m.p. 95.5-101.5° was also isolated; we suggest that it is p-dicyclohexylbenzene.

Optimum conditions could not be found for reactions with p-chloro- and p-bromotoluenes. The main bulk of the organoaluminum compound does not react (the reaction mixture decomposes with intense heat liberation). Here also diphenyl is the main product. Traces of terphenyl and an oily substance were also isolated. The fact that p-chloro- and p-bromotoluenes do not form methyldiphenyls suggests that in these reactions there is dimerization of the phenyl radicals formed on thermal dissociation of phenylaluminum diiodide:

$$2C_6H_5AlI_2 \xrightarrow{245-255°} C_6H_5{-}C_6H_5 + 2[AlI_2]$$

In the absence of aryl halide, however, thermal dissociation does not take place in these conditions (expt. 4, Table 1) and the diphenyl yield is only 13%. This is in accord with our previously obtained data for the interaction of phenylmagnesium bromide with bromobenzene [1]. It may be suggested that the halogenated derivative is necessary for reduction of aluminum subhalide, as is the case in the organomagnesium synthesis in presence of $CoCl_2$ [4]:

$$C_6H_5Br + \cdot AlI_2 \rightarrow C_6H_5\cdot + AlI_2Br.$$

The free phenyl radical either enters into reaction with excess benzene or disproportionates to give polyphenyls [5, 6, 7]. The fate of the p-chlorophenyl radical could not yet be established.

EXPERIMENTAL

The mixture of components was heated in an autoclave. Conditions and results of condensations are set forth in Tables 1 and 2. Below is a description of an experiment giving maximum yields of diphenyl.

Condensation of phenylaluminum diiodide with bromobenzene (expt. 11). Into an autoclave of 100 ml capacity were charged, in a nitrogen atmosphere, 40 ml of a benzene solution (from 70 ml) of $C_6H_5AlI_2$ prepared from 42.8 g C_6H_5I and 4.2 g Al and 30 g bromobenzene [1]. The mixture was heated for an hour at 245-255°. After cooling, the autoclave was opened and the mass run into ice containing hydrochloric acid. The aqueous layer was repeatedly extracted with benzene. The very dark-colored (due to iodine) benzene extract was twice washed with water, with dilute caustic alkali, and again with water. Treatment with alkali caused separation

TABLE 1

Condensation of $C_6H_5AlI_2$ with bromobenzene (30 g)*

No. of expt.	$C_6H_5AlI_2$ from C_6H_5I (in g)	Duration of heating (in hours)	Temperature	C_6H_5Br recovered (in g)	Residue (in g)	Diphenyl (in g)	Diphenyl (in %)
1	20.4	-	-	-	2.1	1.0	13.0
2	22.7	-	-	-	1.6	1.3	14.7
3	10.2	-	-	-	0.9	0.4	10.4
4	15.3	18.0	200-250°, towards the end 300	-	2.25	0.85	14.9
5	20.4	3.5	210-220, towards the end 250**	-	-	Traces	
6	21.7	1.0	220-230, towards the end 250	23.7	21	1.7	20.7
7	18.1	2.0	220-230**	18.6	7.0	4.4	64.7
8	20.4	6.0	220-240	-	-	0.5	6.5
9	16.3	2.0	220-240, towards the end 260	27.7	3.8	2.6	43.0
10	20.4	4.5	220-250, towards the end 260**	-	-	0.5	6.5
11	23.3	1.0	245-255	5.6	14.2	8.6	97.7
12	20.4	0.5	244-256	8.5	12.5	6.9	90.0
13	17.5	1.0	256, towards the end 270**	-	-	0.5	7.5
14	18.1	0.5	250-280***		Not worked up		
15	22.7	0.5	250-300***		Not worked up		
16	18.1		Rapidly to 300	26.5	5.5	3.5	45.4

TABLE 2

Condensation of $C_6H_5AlI_2$ with p-chloro- and p-bromotoluenes

No. of expt.	$C_6H_5AlI_2$ from C_6H_5I (in g)	ArX (in g)	Solvent	Duration of heating (in hours)	Temp.	ArX recovered (in g)	Residue (in g)	Diphenyl (in g)	Diphenyl (in %)
1	16.8	32.1	p-Chlorotoluene	0.7	95-160°	27.0	1.3	0.8	15.7
2	20.4	32.1	Benzene	15.0	140-150	28.9	1.7	1.0	13.0
3	20.4	26.7	p-Chlorotoluene	11.5	170-180	16.0	2.1	1.1	14.3
4	20.4	32.1	p-Chlorotoluene	14.5	200-205	20.3	-	2.0	26.0
5	20.4	26.7	Benzene	6.0	200-240, toward end 260	-	-	2.1	27.3
6	20.4	32.1	p-Chlorotoluene	10.0	240-260**	-	-	0.5	6.5
7	20.4	20.8*	Benzene	0.7	246-252	17.5	2.2	1.4	18.2
8	20.4	21.4	Benzene	0.8	248-252	14.5	3.8	2.3	30.0
9	20.4	12.8	Benzene	0.75	250-258	9.9	2.5	1.7	22.1
10	20.4	21.4	Benzene	0.5	244-252	-	2.0	1.5	19.4
11	20.4	20.8*	Benzene	0.7	256-268**	-	1.2	1.1	14.3
12	20.4	20.8*	Benzene	1.0	244-261**	-	0.6	0.4	5.2
13	21.3	32.1	p-Chlorotoluene	10.0	250-300***	-	-	-	-
14	20.4	16.0	p-Chlorotoluene	13.0	300-320***	-	-	-	-

TABLE 1:
* Experiments 1 to 4 without bromobenzene.
** Reaction product (resinous mass) steam-distilled.
*** Complete charring of reaction products.

TABLE 2
* Experiments performed with p-bromotoluene
** Reaction product (resinous mass) steam-distilled.
*** Complete charring of reaction products.

of a brown precipitate which was filtered off. After drying with calcium chloride, the benzene was distilled off followed by the bromobenzene up to 200° (4 g recovered). The residue (14.2 g) was distilled in vacuum to give the following fractions (at 40 mm): 1) b.p. up to 110° (mixture of bromobenzene and diphenyl), 1.6 g; 2) b.p. 140-210°, 8.6 g. From the residue at 0.2 mm was obtained a crystalline fraction 3) with b.p. up to 360°, 0.6 g.

Refractionation of fractions 1) and 2) yielded crude diphenyl with b.p. 140-150° at 35 mm (6.4 g) and a substance with b.p. 140-145° at 4 mm (2.4 g). The diphenyl fraction was fractionally crystallized from ethanol. Diphenyl was isolated with m.p. 69.5-70° [8]; it did not give a melting point depression with an authentic specimen. A small amount of oil (a) was obtained. The fraction with b.p. 140-145° at 4 mm and m.p. 76-82° was crystallized from methanol. An oil b was obtained (which was mixed with oil a) and crystals with m.p. 89-90°. Their fractional crystallization from dilute ethanol gave a substance (A) with constant m.p. of 95.5-100° and a pleasant, orangey odor (presumably p-dicyclohexylbenzene).

Fractionation of oils a and b gave: diphenyl with b.p. 116-121° at 8 mm (0.7 g), substance (A) with b.p. 121-128° at 2 mm (0.8 g), an oil with b.p. 132-140° at 2 mm (0.6 g) and terphenyl mixed with oil with b.p. 160-200° at 2 mm (0.9 g).

The 3rd fraction with b.p. up to 360° at 2 mm was dissolved in a large excess of hot ethanol. Terphenyl with m.p. 199-201° came down on cooling. After sublimation and two recrystallizations from benzene the m.p. was 206-207° [8]. A mixed test with an authentic specimen of terphenyl does not give a melting point depression. A portion of the crystals, insoluble in ethanol, melts at 301°. The crystals which adhered to the condenser and the resin which remained in the flask were extracted with hot benzene; addition of ethanol brought down a light-brown flocculent precipitate with m.p. 268°. Two sublimations gave white crystals with m.p. 288°. The mixture of high-melting crystals was digested with a 20-fold excess of benzene in order to remove the terphenyl. A substance with m.p. 317-318° was isolated which from the conditions of isolation and the melting point is identified as quaterphenyl [8].

The brown precipitate, filtered from the benzene extract of the condensation product, was sublimed to give quinquephenyl with m.p. 372°. The literature [7] reports 370° for the sublimed product and 388.5° after washing and recrystallization from quinoline.

The same products were obtained in expt. 12. Diphenyl with b.p. 104-110° at 5 mm (6.9 g).

Condensation of phenylaluminum diiodide with p-chlorotoluene (expt. 8). Reactants were a 40 ml benzene solution of $C_6H_5AlI_2$ (from 80 ml), prepared from 42.8 g C_6H_5I and 4.2 g Al, and 21.4 g p-chlorotoluene. The mixture was heated at 248-252° (mainly at 250°) for 50 minutes. Considerable heat is evolved when the reaction mixture is decomposed. 14.5 g p-chlorotoluene (up to 200°) was recovered. Fractionation of the residue (3.8 g) gave the following fractions: 1) b.p. up to 120° at 100 mm, 0.6 g; 2) b.p. 116-120° at 12 mm, 2.3 g (diphenyl); 3) b.p. 170-230° at 8 mm, 0.7 g (crystals mixed with oil). From the latter fraction was isolated terphenyl with m.p. 199-200°, not giving a depression of melting point with an authentic specimen.

SUMMARY

1. The condensation of phenylaluminum diiodide with bromobenzene, p-chlorotoluene and p-bromotoluene was studied.

2. Optimum conditions were found (heating in autoclave for an hour at 245-255°) for preparation of diphenyl in a yield of 90% of the theoretical from the reaction of $C_6H_5AlI_2$ with bromobenzene. By-products identified were terphenyl, quaterphenyl and quinquephenyl.

3. It was shown that the main product in condensations of $C_6H_5AlI_2$ with p-chloro- and p-bromotoluenes is diphenyl (up to 30% of the theoretical).

4. It is suggested that interaction of $C_6H_5AlI_2$ with aryl halides proceeds by a radical mechanism resulting from thermal dissociation of $C_6H_5AlI_2$.

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THE HYDROGEN BOND AND THE PHYSICAL PROPERTIES OF 8-HYDROXYQUINOLINE

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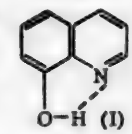
The presence of an intramolecular hydrogen bond in 8-hydroxyquinoline (I) is demonstrated by a series of properties: low area of molar absorption of the OH group in the infrared region [1], low acidity [2], facility of formation of inner-complex salts [3]. For the purpose of clarifying the influence of this type of bond on the physical properties of 8-hydroxyquinoline, determinations were made of density, surface tension and viscosity at 209° of 8-hydroxy- and 8-methoxyquinolines, also of the viscosity of quinoline (table). In the table are also set forth data for the boiling point of quinoline and some of its hydroxy and methoxy derivatives.


(I)

Physical Properties of Hydroxy- and Methoxyquinolines

Compound	Absolute b.p.	d_4^{209}	γ (209°)	$\eta\ 10^3$ (209°)
Quinoline	511	0.937[4]	24.7[4]	3.90
4-Hydroxyquinoline	573	–	–	–
6-Hydroxyquinoline	>633	–	–	–
8-Hydroxyquinoline	540(752)	1.034	28.1	5.27
6-Methoxyquinoline	578(740	1.000	–	–
8-Methoxyquinoline	555(750)	1.012	28.0	6.04

It follows from the data obtained that formation of an ether from 8-hydroxyquinoline, as in the case of substituted phenols with a stable intramolecular hydrogen bond [5], brings about a rise of viscosity with rising boiling point and hardly any change in surface tension. Compared with its isomers, 8-hydroxyquinoline possesses a much lower boiling point (a similar difference was observed in the above-mentioned disubtituted benzenes), while its isomers possess – in contrast to 8-hydroxyquinoline – a much higher boiling point in comparison with their methyl ethers. Like o-nitrophenol in relation to nitrobenzene, 8-hydroxyquinoline exhibits a relatively small rise of the above constants over quinoline. In this connection, as is also characteristic of substituted benzenes with an intramolecular hydrogen bond [5], the relative rise of density on introduction of a hydroxyl into quinoline in the 8-position appreciably lags behind the relative rise of molecular weight (1.110 and 1.124 respectively).

Consequently the physical properties of 8-hydroxyquinoline are in harmony with the concept of the presence in its molecule of a stable hydrogen bond. The regularities established for substituted benzenes in respect of various physical properties of inter- and intramolecularly associated compounds prove to be applicable also to the correspoding heterocyclic compounds.

EXPERIMENTAL

Quinoline was purified by two distillations and collection of the 232° (754 mm) fraction. 8-Hydroxyquinoline, white needles with m.p. 75° was purified by distillation and recrystallization from ethanol-water mixture. 8-Methoxyquinoline [6] was prepared by methylation of 8-hydroxyquinoline with methyl iodide in methanol; it was purified by distillation, b.p. 281-282° (750 mm).

The procedures for determination of density, viscosity and surface tension have been described already [5]. The pycnometer and capillaries were calibrated against quinoline. The liquid used for establishment of a constant temperature in the vapor thermostat [7] was nitrobenzene.

SUMMARY

1. Determinations were made of the density, surface tension and viscosity at 209° of 8-hydroxy- and 8-methoxyquinolines.

2. It was shown that the regularities characteristic of the physical properties of substituted benzenes with an intramolecular hydrogen bond are also observed in the corresponding heterocyclic compounds.

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THE NUMBER OF LINEAR AND CYCLIC α-AMINOACID BONDS IN THE PROTEIN MOLECULE

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With reference to a whole series of examples we showed [1,2,8] the possible existence in the protein molecule of the following structures: amidine, N-amino-acylpiperazine, amidino-aminoacyl, and carbonnhydride. The synthesis and examination of the properties of these structures enable already the establishment of the principal valency bonds in the protein molecule, which abroad are regarded as linear anhydride bonds.

According to the polypeptide theory of proteins there exists a chain molecule whose length with bonds of the valency type is within the range of 300-20000 amino acids. The whole diversity of protein forms, on the hypothesis of a linear-anhydride structure, is explained by spiral coiling of this gigantic chain or to formation of diverse loops. The latter explanation, however, fails to account for the lability and other properties inherent in proteins.

In opposition to the above-mentioned theory, we suggest, on the basis of experiments, that protein is a polymer of a complex anhydride (monomer) built up from 5-8-16 amino acids. This polymer is formed by the joining together, with the help of supplementary valencies, of an integral number of molecules of the original low-molecular (M about 1000) micromolecule. It is not excluded that in this type of compounds there are present in equilibrium in a variety of states all the fragments of the micromolecule (monomers) that we obtained. Consequently the anhydride-polymer hypothesis advanced by one of us (N.I. Gavrilov) refutes the existence of the long polypeptide chain and reduces the polypeptide portion of the protein molecule to the size of three amino acids. Such a linear anhydride is linked to the cyclic anhydride, diketopiperazine, amidine and aminoacyl forms of linkage. The result is a linear-cyclic anhydride and a structural micromolecule is developed which further polymerizes into a macromolecule. The micromolecule is very active and capable of a number of transformations.

Kober [3] was the first to point out that the absorption curve of the copper complex of protein strongly resembles the absorption curve of a tripeptide. Jesserer and co-workers [4] attempted to characterize the structure of protein with the aid of "copper numbers". On the erroneous assumption that the "violet" protein complex, in their opinion, is obtained by mixing the "red" complex of the same protein with the blue color of the copper cation present in the complex, they could not utilize the biuret reaction for problems of protein structure.

The biuret reaction was again applied by Plekhan [5] to the elucidation of the structure of protein and with its aid were established all the regularities of the structure of the copper biuret complexes of peptides.

In this paper we attempt a quantitative comparison of the participation of tripeptides and diketopiperazines (Table 5) in the building up of the protein micromolecule. Our task was hindered by the presence in protein of a large number of prosthetic groups, sometimes of unknown structure. In proteins containing phosphoric or sulfuric acids (casein, sturin sulfate), glucosamine (albumin), and a small amount of carbohydrates (edestin, etc.), corrections for their quantity give very satisfactory results by comparison with experimental data and theory. We also found difficulty in establishing the number of amino acids in the large polymeric molecule and in connection with the inconstancy of its amino acid composition [6]. We succeeded, nevertheless, in making the desired comparison to a rough approximation in the case of a series of proteins, excluding gelatin.

For the quantitative content of cyclic forms of bonds in proteins we made use of data from papers by Koperine [2] and Ioanisiani [7] who used the electroreduction method. For all proteins with a known content of cyclic bonds we determined the "copper numbers"*, which for casein agreed with the value previously obtained by Plekhan [5].

*Plekhan defines the copper number as the amount of protein in grams which binds 1 g-atom of copper to form the copper complex. A titrimetric method was also proposed for determination of copper numbers [5].

Into the "copper number" enters: 1) 1 mole protein tripeptide composed of three amino acids of average (for a given protein) molecular weight; 2) a corresponding proportion of diketropiperazine required for the three amino acids of the tripeptide. The amino acid weight of the diketopiperazine was calculated from the mean relative amount of amino acids entering into its composition, i.e. phenylalanine, proline, serine, and leucine, and partly from the corresponding amounts of alanine and glycine; 3) the mean weight of non-amino acid components of the given protein, i.e., sulfuric and phosphoric acids, carbohydrates and glucosamine recalculated to 3 + 2x amino acids (x being the proportion of diketopiperazine required for the tripeptide) and calculated according to their percentage ratio in the whole of the protein molecule.

For all proteins the calculated "copper numbers". allowing for the prosthetic groups, agreed in the majority of cases with the experimental values.

This agreement enables us to postulate: 1) The existence of the cyclic forms of bonds in the protein molecule; 2) the presence of three amino acid fragments in the peptide portion of the structure of the protein molecule.

In the present investigations we made no reference to the amidino-acyl forms of bond which we not only discovered in the case of model structures but also proposed as components of the structure of the antibiotic gramicidin C. The role of the carboanhydride bond, actualized synthetically, still remains obscure, since it likewise found no reflection in the quantitative determination of diketopiperazines and tripeptides in the protein molecule. We hope to develop these aspects in later experiments.

EXPERIMENTAL

Our investigations on the determination of copper numbers were carried out on proteins on which preliminary determinations were made of the number of cyclic forms of bonds. The sturin -sulfate and blood albumin which we used were analyzed by A.V. Koperine. Our sturin sulfate was prepared by N.N. Yarovenko from the milt of Russian sturgeon by the combination method of Kossel [9] and Malenük [10].

Blood albumin was isolated from human blood, purified by dialysis and precipitated with acetone in the cold. The casein used was commercial Kahlbaum materials (Hamarsten's grade). We prepared gliadin from wheat gluten and purified it by repeated reprecipitation from aqueous ethanol and from a mixture of ethanol and ether. Photographic gelatin was purified by Leb's method; at 110° its water content was found to be 13.5%. Gramicidin C was recrystallized from aqueous ethanol.

Preparation of Copper Biuret Solutions of Proteins

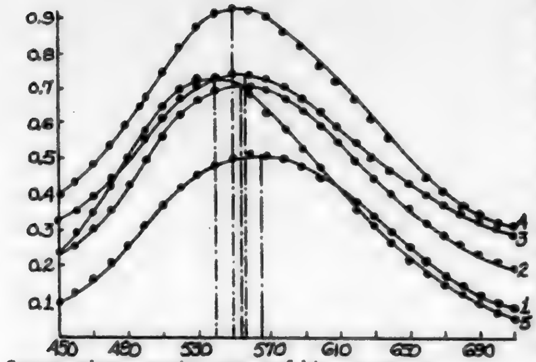
To a weighed amount of about 0.2 g protein were added 10 to 15 ml 2% $CuCl_2$ solution and 25 to 30 ml 2% NaOH solution. After standing for an hour the excess copper hydroxide was removed by centrifuging and definite volumes, containing 0.025-0.030 g protein, i.e. 0.25-0.30% solutions, were taken for spectrophotometric measurements. The spectrophotometric curves were plotted with the help of the SF-4 spectrophotometer.

Determination of Copper in Copper Biuret Solutions of Proteins

The copper biuret solution of protein was centrifuged and 15 to 25 ml transparent solution of the copper complex, containing 0.1-0.15 g original protein was taken This solution was ashed with 4 ml conc. sulfuric acid by the Kjeldahl method. After combustion. the contents were transferred into 50 ml water in a flask and titrated iodometrically for copper with 0.5 N thiosulfate solution. In Table 1 are set forth the values of the optical densities of the proteins investigated by us; the diagram shows the spectrophotometric curves of these proteins.

The amount of peptide nitrogen (the nitrogen of the α-amino groups) is calculated by multiplying by 14 the amount of amino acids in the molecule of the given protein (as calculated for example from Tristram's tables [6]) and dividing the resultant number per g nitrogen into 10^5 g protein. From the α-amino nitrogen by deduction of the nitrogen of the cyclic forms of bonds we find the nitrogen of the peptide forms of bonds. By determination of the percentage ratio of peptide nitrogen to cyclic nitrogen we arrive at the relative amounts of cyclic and linear α-amino nitrogen. From these ratios we calculate the proportion of cyclic nitrogen required for the three nitrogens of the tripeptide. To the number of the average amino acid residue in the tripeptide we add the mean amino acid residue in the cyclic forms of bonds calculated on the basis of the ralative amounts in the protein molecule of proline, hydroxyproline, phenylalanine, leucine and (in part) alanine and glycine, which are most frequently met with in rings.

For sturin sulfate. As an example we give the procedure for determining the average molecular weight of the amino acid entering the ring. Of all the amino acids of sturin sulfate, leucine, alanine, and serine participate in the cyclic forms of the bond in the ratio of 1:2:2, i.e. 5 amino acids in all. By multiplying the molecular weights of these amino acids by their number, adding them all and dividing by 5, we obtain the mean



Spectrophotometric curves of biuret copper complexes of proteins

1) Gelatin max.(565 mμ), 2) edestin (555 mμ), 3) casein max: (552.5 mμ), 4) blood albumin (550 mμ), 5) sturin -sulfate (540 mμ).

residual weight of the amino acid in the peptide. This number is equal to 109.4. and without water to 91.4. 10 molecules of arginine. 2 molecules of histidine and 3 molecules of lysine are linked in the peptides, and these 15 amino acids of basic character are combined with 8 molecules of sulfuric acid. The total molecular weight of these amino acids together with the 8 molecules of sulfuric acid is 3273. Hence the average residual weight of the amino acid participating in the peptide forms of the bond is equal to 3273: 15 = 218, or 200 (without water). In the case of proteins containing moisture, the α-amino nitrogen must be calculated with allowance for the real content of total nitrogen in the protein examined.

The copper number of sturin sulfate is calculated by adding together the average residual weights of the amino acids in the ring and in the tripeptide, i.e. 600 + 91.4 or 691.4.

TABLE 1

Optical Densities of Copper Biuret Complexes of Various Proteins

Wave length (in mμ)	Concentration of solutions (in %)						
	0.32	0.25	0.36	0.22	0.25	0.25	0.25
	sturin-sulfate	casein	albumin	proto-acid	gliadin	edestin	gelatin
450	0.236	0.133	0.268	0.113	0.136	0.182	0.092
460	0.286	0.166	0.308	0.138	0.158	0.221	0.126
470	0.350	0.211	0.366	0.176	0.201	0.271	0.168
480	0.426	0.268	0.442	0.224	0.247	0.331	0.217
490	0.508	0.332	0.514	0.275	0.298	0.402	0.271
500	0.584	0.403	0.606	0.327	0.361	0.484	0.324
510	0.651	0.467	0.684	0.380	0.419	0.561	0.377
520	0.693	0.528	0.754	0.430	0.470	0.623	0.424
530	0.718	0.572	0.800	0.465	0.509	0.682	0.460
540	**0.731**	0.599	0.822	0.486	0.534	0.708	0.488
545	0.721	0.608	–	0.491	–	0.717	0.496
550	0.718	**0.615**	0.832	**0.493**	0.537	0.719	0.508
555	0.702	**0.615**	0.826	**0.493**	0.544	**0.721**	0.511
560	0.671	0.609	0.822	0.489	0.539	0.711	0.513
565	–	–	–	0.488	–	–	**0.513**
570	0.636	0.598	0.792	0.481	0.527	0.701	0.513
580	0.558	0.585	0.764	0.463	0.501	0.675	0.503
590	0.541	0.576	0.714	0.445	0.481	0.638	0.486
600	0.481	0.549	0.662	0.412	0.445	0.589	0.461
610	0.428	0.508	0.604	0.377	0.405	0.527	0.425
620	0.361	0.462	0.546	0.341	0.363	0.483	0.387
630	0.312	0.420	0.474	0.299	0.316	0.407	0.344
640	0.265	0.371	0.412	0.267	0.281	0.367	0.298
650	0.222	0.327	0.354	0.232	0.244	0.316	0.256
660	0.190	0.273	0.304	0.197	0.211	0.267	0.217
670	0.157	0.233	0.256	0.167	0.183	0.226	0.184
680	0.092	0.197	0.218	0.142	0.156	0.187	0.155
690	0.083	0.167	0.190	0.124	0.136	0.158	0.128
700	0.069	0.147	0.162	0.106	0.116	0.133	0.107
710	0.058	0.119	0.138	0.098	0.099	0.113	0.087

For gliadin. Of the 855 amino acids entering into 10^5 g protein, ammonia constitutes 321 molecules, arginine 15.75, histidine 11.75, lysine 4.45, and tryptophane 3.0 molecules. Arginine contains 42 g non-amino

nitrogen in the molecule, i.e. in all 15.75 x 42 = 661.5 g; histidine has 11.75 x 28 = 329.0 g non-amino nitrogen; lysine contains 4.45 x 14 = 62.3 g amino nitrogen; tryptophane has 3 x 14 = 42 g. Ammoniacal nitrogen = 321 x 14 = 4494 g. The total of α-non-amino nitrogen and ammoniacal nitrogen in gliadin is 1655 + 4494 = 6149 g, equivalent to 34.8% of the total nitrogen. Our calculation thus gives a content of α-amino nitrogen in gliadin of 65.2%, which recalculated to total nitrogen in the investigated protein (16.40%) gives a figure of 60.53%. The nitrogen in the cyclic forms in gliadin constitutes, according to the data of Ioanisiani [7], 26.5% of the total nitrogen. From the difference between the α-amino nitrogen and the cyclic nitrogen we get a figure of 34% for the nitrogen of the peptide forms of the bonds. We then calculate the relative amounts of cyclic and peptide nitrogen (in relation to the α-amino nitrogen). The values are 43.83% for the rings and 56.15% for the peptides. Hence the amount of cyclic forms of the bonds required for the tripeptide is represented by the number 2.34. From the average weights of the amino acids entering into the ring and the "tripeptide" and set forth in the table, we find a copper number for gliadin of 545.9.

For gelatin. Out of the 1100 amino acids entering into 10^5 g protein we calculate the α-amino nitrogen from the difference between 100 and the α-non-amino nitrogen. The α-non-amino nitrogen comprises the sum of the nitrogens of arginine (49.2 x 42 = 2066.4), histidine (4.71 x 28 = 131.88), lysine (31.5 x 14 = 441.0) and ammonia (5.3 x 14 = 74.2) and is equal to 2713.48 or 15.06% of the total nitrogen. Hence the α-amino nitrogen of gelatin is equal to 84.9%, or recalculated to the total nitrogen of the actual protein (16.24%) the α-amino nitrogen amounts to 76.6%. The cyclic nitrogen of gelatin, according to electroreduction data, is 23.5%. From the difference between the α-amino nitrogen and the cyclic nitrogen we find a value of 53.1% for the nitrogen of the peptide groups. We then calculate the relative amounts of linear and of cyclic nitrogens to α-amino nitrogen, the respective values being 69.33 and 30.68%. Hence the number of rings required for a tripeptide is expressed by the number 1.33.

Of all the amino acids of gelatin the rings contain proline, hydroxyproline, phenylalanine and glycine in the following amounts: proline + hydroxyproline 134.5 moles; phenylalanine 25 moles; glycine 109 moles. The total molecular weight of these acids is 28859, and therefore the average molecular weight of the amino acids associated with the ring is obtained by dividing 28859 by the sum of all the amino acids of the ring (268.5 moles) and is equal to 107 or, with deduction of water, 89. The average molecular weight of the amino acids in the peptides is 73.2. The copper number of gelatin is equal to 383.6 after allowing for the water, which comprises 13.5% of the total weight of gelatin.

For albumin. From the 846 amino acids entering into 10^5 g protein, we calculate the α-amino nitrogen from the difference between the α-non-amino nitrogen and 100. The α-non-amino nitrogen is determined from the sum of the nitrogens of arginine (35.7 x 42 = 1499.4), histidine (22.6 x 28 = 632.8), lysine (84.3 x 14 = 1180.2) and ammonia (63 x 14 = 882) and is equal to 4194.4 or 26.29% in relation to the total nitrogen of albumin. Hence the α-amino nitrogen of albumin is 73.71%. The cyclic nitrogen in albumin is 21.6% of the total nitrogen of the protein; consequently the figure for peptide nitrogen is 52.11%. The relative amounts of linear and cyclic forms of the bonds are expressed by the numbers 70.68 and 29.30, while the number of rings required per tripeptide is represented by the number 1.24.

The copper number of albumin taking into account the average molecular weights of the amino acids in the ring and the peptide set forth in Table 1, is 463.6.

For casein.* The α-amino nitrogen of casein, according to Hamarsten, calculated from the amino acid composition and a total nitrogen content of 15.76%, is equal to 73.79%. Conversion to the total nitrogen of the investigated protein (14.80%) gives a figure of 69.29%. The cyclic nitrogen content of casein (22.9% of the total nitrogen) enables determination of the nitrogen of the peptide groups (46.4%). The relative amounts of linear and cyclic forms of bonds in casein in relation to the α-amino nitrogen are expressed by the numbers 66.95 and 33.05% respectively. Hence the number of rings per tripeptide is calculated from the expression:

$$x = \frac{33.05 \cdot 3}{66.95} = 1.5.$$

The copper number of casein is the sum of the average molecular weights of the 3 amino acids in the peptide and of the 1.5 amino acids in the ring together with the quotas of carbohydrate group and phosphoric acid; it is equal to 565.4.

*The α-amino nitrogen of proteins, calculated from the amino acid composition and the total nitrogen, agrees with that calculated on the basis of amino acids containing also nitrogen in other forms than that of α-amino nitrogen.

For edestin. The α-amino nitrogen of edestin, taking into account its amino acid composition and total nitrogen, is 58.43%. Ring nitrogen in edestin is represented by 18.1% and peptide nitrogen by 40.33%. The relative amounts of rings and peptides are determined from the ratios of their absolute amounts of amino acids: 1 molecule of proline, 3 of leucine and 1 of phenylalanine. The total of the molecular weights of all these amino acids is 673.53, so that the mean molecular weight of the amino acid associated with the ring is 134.7 or (allowing for water) 116.7. The average molecular weight of the amino acid in the peptides is 99.4. The copper number of edestin is the sum of the molecular weights of the amino acids in the ring and tripeptide, allowing for the non-amino nitrogen of the prosthetic groups, and is equal to 486.

For gramicidin. The amino acid composition of gramicidin hydrochloride is: valine (M 117.1), proline (M 115.08), leucine (M 131.11), phenylalanine (M 165.09), and ornithine (M 132.13) in amounts of 2 moles (for dimer). The α-amino nitrogen derives from 10 amino acids present in the gramicidin molecule, while the α-non-amino nitrogen is represented by the two nitrogens of ornithine. In Table 2 we set forth the results of copper determination and of theoretical calculations of the copper numbers. In column 4 the nitrogen of the α-amino groups is calculated in relation to the total nitrogen in the same protein which we analyzed.

For sturin -sulfate, blood albumin, edestin and gramicidin, the nitrogen of the α-amino acids corresponds to the anhydrous preparations. In column 6 the amount of cyclic nitrogen is given as a percentage of the total nitrogen of the α-amino groups, which also represent the main skeleton of the monomer or polymer of the protein, characterizing its participation in the total structure of the protein molecule. Columns 6 and 8 show the relative numbers of cyclic and linear bonds in the protein molecule; in all cases the linear bonds predominate over the cyclic. This relation is quantitatively expressed in column 9. Only gelatin gave copper numbers higher than the theoretical. An attempt to explain this phenomenon, by analogy with gramicidin, by formation of a complex in course of time was not justified. The copper number of gelatin determined 30 minutes after the instant of formation of the copper complex was 489.0. The copper number 48 hours after the start of the reaction was 487.

EVALUATION OF RESULTS

On analyzing the results of the investigations summarized in Table 2 both from the aspect of the number of linear forms of bonds and from that of the content of cyclic structures, we can recognize the important role of the latter in the structure of protein. Thus, in sturin-sulfate one quarter of the α-amino bonds (24%) are cyclic and 44% of these bonds are in gliadin. Consequently the diketopiperazine theory advanced by N.D. Zelinsky and V.S. Sadikov, expressing the important role of cyclic anhydrides, has found further confirmation in a quantitative study of protein structure. In proteins on the average about 33% of the α-amino nitrogen is present in derivatives of piperazines.

The uncertainty about the tripeptide structure with a linear-anhydride character (peptide) has also been fully cleared up in our research. Thus in proteins about 70% of the α-amino nitrogen is present in linear forms of the amino acids system.

The N-aminoacyl form of linkage, experimentally demonstrated by us in the structure of gramicidin C, is still the object of research and evaluation in the case of proteins. In this connection attention may be drawn to the role of the amidine linkage which stabilizes the piperazine-tripeptide structure in the protein monomer. This circumstance must be taken into consideration when separating protein from its system. This form of linkage leads us on the basis of the data of the present investigation to suggest a possible participation of the linkage in question both in the formation of monoamidino-piperazinic structures and in the formation of structure (II). This conclusion is suggested by an analysis of the number of amino acids present in rings and peptides (Table 5).

From these considerations it follows that for each tripeptide in gramicidin there is present 1 piperazine, and that 1 piperazine in sturin is linked to 2 tripeptides. In the remaining proteins we have extremely complex associations of tripeptides with rings, to a considerable extent approximating to system (II) see section below on structure of gramicidin).

Structure of Gramicidin

As we know, apart from "violet" copper complexes, proteins also form "red" complexes (Table 3). Unfortunately these "red" complexes have not yet been adequately investigated with reference to the characterization of their fourth nitrogen.

We suggest that the fourth nitrogen atom may be:

1) The nitrogen of amides of tripeptides containing dicarboxylic acids.

TABLE 2

Protein	Number of acids	Total nitrogen (%)	Nitrogen of α-amino groups to total nitrogen (%)	Nitrogen of cyclic forms of bonds (%): total nitrogen *	Nitrogen of cyclic forms of bonds (%): α-amino group nitrogen	Nitrogen of peptide forms of bonds (%): total nitrogen	Nitrogen of peptide forms of bonds (%): amino group nitrogen	Number of amino acids in ring/β amino acids in peptide	Average weight of amino acids: in peptide	Average weight of amino acids: in ring	Weight of prosthetic groups (carbohydrates, phosphorus, sulfur)	Grams protein combining with 1 g-atom copper: calculated	Grams protein combining with 1 g-atom copper: found
Surin-sulfate	579	23.37	35.10	8.4	23.93	23.70	78.63	1	200	91.4		691.4	691; 683
Blood albumin	846	15.95	73.71	21.6	29.30	52.11	70.68	1.24	100.2	131.1	0.5 carbohydrate	463.6	453; 462
Casein, Hamarsten's data (15.76)	831	14.80	69.29	22.9	33.05	46.4	66.95	1.5	119.1	120	25 phosphorus, carbohydrates 3.1	565.4	568; 569
Gliadin (17.66)	855	16.40	60.53	26.5	43.83	34.0	56.15	2.34	98.2	107.4		545.9	559; 576
Edestin	827	18.55	58.43	18.1	30.94	40.33	69.05	1.34	99.4	116.7	1.7% or 31.1 non-amino nitrogen (on total)	486	486; 489
Gelatin (18.0)	1100	16.24	76.6	23.5	30.68	53.1	69.33	1.33	73.2	89	13.5% water	383.6	489; 487
Bramicidin	10	13.25	33.4	33.2	40.0	50.2	60.19	2	108.8	122.1	36.5% hydrochloric acid and 36 water	643	646

* As determined by the method of Koperina and Ioanisian.

It has been shown [5] that a tripeptide containing asparagine shifts the maximum of absorption in the direction of short waves. It is not excluded that proteins, which contain considerable amounts of asparagine, utilize the amido nitrogen of this amino acid in the formation of the copper complex, for example in the case of gliadin.

2) Derived from acylamino structures in which the nitrogen of piperazine starts to function as amide nitrogen (piperazide), as in the structure of gramicidin C.

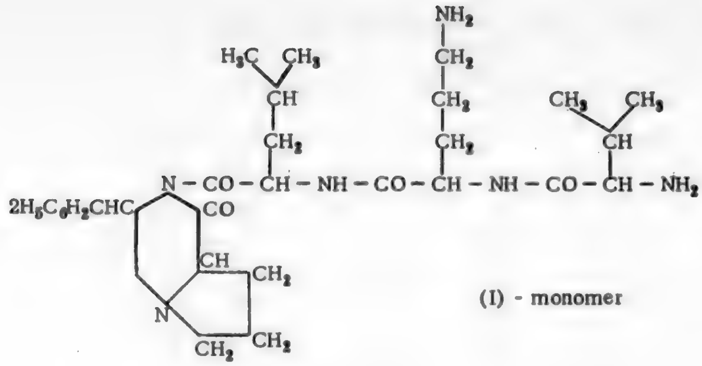
3) The nitrogen of penta- and hexapeptides present in the protein molecule.

4) Finally, as shown by Plekhan, functional groups of amino acids: the amidine nitrogen of histidine and the β-hydroxy group of threonine [5] can shift the absorption maxima in the direction of short waves.

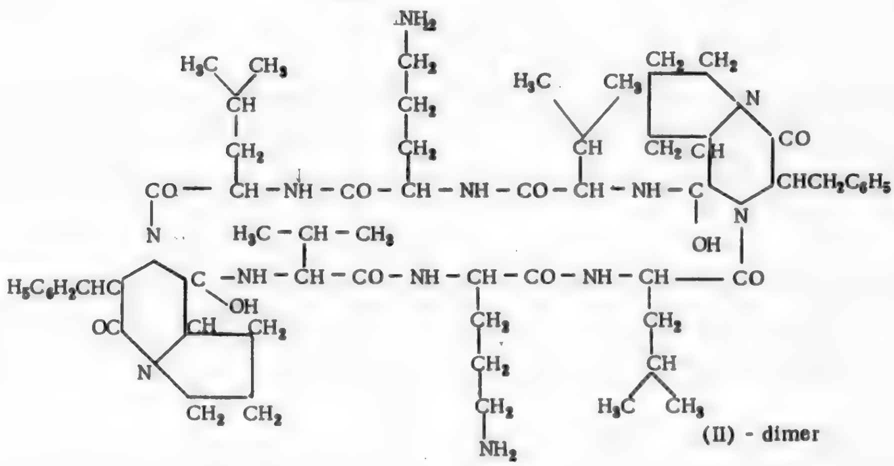
Up to now we have no conclusive proof of participation of the fourth nitrogen in the copper complex according to one of the above-submitted structures. Only investigations on models containing the above-submitted structures in conjunction with piperazine structures and with participation of known forms of linkages (peptide, cyclic, amidine and acylpiperazine) and comparison with proteins will give the key to solution of this interesting problem.

Concerning the copper numbers of protein (Table 4), these actually express the numbers of both linear and cyclic groupings in the protein molecule.

Consequently from the ratios of amino acids bound in cyclic and linear anhydrides and with utilization of the formula of one of the authors (N.I. Gavrilov) we can derive the amino acid composition of the monomers of individual proteins (Table 5).



(I) - monomer



(II) - dimer

TABLE 3

Maxima of Absorption of Solutions of Copper Biuret Complexes of Proteins and the Amount of "Violet" and "Red" Complexes Present in them, Calculated from an Artificial Mixture of Peptides

Protein	Absorption maximum (in mμ)	Percentage of "red" complex calculated from a mixture of		Percentage of "violet" complex calculated from a mixture of	
		penta- and tripeptide	tetra- and tripeptide*	penta- and tripeptide	tetra- and tri-peptide*
		515/570	525/570	515/570	525/570
Sturin sulfate	540	54	30	46	70
Blood albumin	550	39	13	61	87
Hamersten's casein	550-555	31	10	69	90
Gliadin	555	30	7	70	93
Edestin	555	30	7	70	93
Gelatin	565	15	2	85	98
Gramicidin	535	38	62	62	38

SUMMARY

1. A number of proteins were characterized on the basis of their copper numbers and determination were made of the cyclic forms of linkages in their structure and of the absorption spectra of the copper complexes.

2. The determined copper numbers of the proteins quantitatively reflect the participation in the structure of protein of linear and cyclic forms of bonds.

3. Analysis of the absorption curves leaves open the question of the sources of the complexes formed by copper with four atoms of nitrogen.

*From M.I. Plekhan's curve

TABLE 4

Absorption Maxima and Copper Numbers of Solutions of Biuret Complexes of Proteins and Gramicidin

Protein	Absorption maxima (in mμ)	Each mole copper requires protein (in g)		
		Calculated	Found	
			by M.I. Plekhan	by us
Sturin sulfate	540	691.4	-	691;683
Blood albumin	550	463.6	394	453;462
Hamersten's casein	550-555	532.0	570	568;569
Gliadin	555	520	-	559;576
Edestin	555	486	-	486;489
Gelatin	565	383.6	547	489;487
Gramicidin	535	643	-	646

TABLE 5

Amino Acid Composition, Number of Rings and Tripeptides in Monomers of Various Proteins and Gramicidin

Protein	Number of amino acids in:		Multiplier	Number of amino acids in:		Number of amino acids in monomer from formula A = 2x + 3y, where x is number of rings and y is number of tripeptides
	ring	peptide		ring	peptide	
Sturin sulfate	1	3	2	2	6	$A = 2 \cdot 1 + 3 \cdot 2 = 8$
Blood albumin	1.24	3	8	10	24	$A = 2 \cdot 5 + 3 \cdot 8 = 34$
Hamersten's casein	1.5	3	4	6	12	$A = 2 \cdot 3 + 3 \cdot 4 = 18$
Gliadin	2.34	3	6	14	18	$A = 2 \cdot 7 + 3 \cdot 6 = 32$
Edestin	1.34	3	3	4	9	$A = 2 \cdot 2 + 3 \cdot 3 = 13$
Gelatin	1.33	3	3	4	9	$A = 2 \cdot 2 + 3 \cdot 3 = 13$
Gramicidin	2	3	1	2	3	$A = 2 \cdot 1 + 3 \cdot 1 = 5$

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INNER COMPLEX SALTS OF AZO COMPOUNDS

I. COMPLEX SALTS OF COPPER WITH SOME o-MONOHYDROXYAZO COMPOUNDS

V. I. Mur

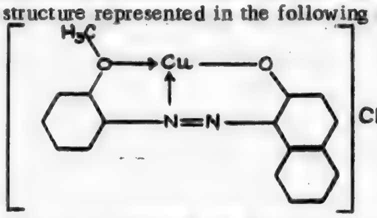
Among the inner complex salts of azo compounds with copper, a special group comprises the complexes of o-monosubstituted compounds in which the salt-forming groups are OH, NH_2 and COOH. Unlike copper complex salts of o,o'-disubstituted azo compounds, in which the o-substituents are the same salt-forming groups and into the composition of which enters 1 atom of copper per molecule of azo compound (1: 1 complexes) [1,2], copper salts of non-sulfonated o-monosubstituted azo compounds contain 1 atom of metal per two molecules of azo compound (1: 2 complexes) [1-10]. Non-sulfonated copper complexes of the simplest o,o'-disubstituted azo compounds of the above-mentioned type were prepared by interaction of ethanolic solutions of the corresponding azo compounds with copper chloride [2], and complexes of o-monosubstituted compounds by interaction of an ethanolic solution of azo compound with an aqueous ammoniacal solution of copper sulfate, or by interaction with the metal in the finely divided state [2-10].

In a study of the relation between structure and some properties of copper complexes of azo compounds, we repeated the experiments of the previous investigators [2] and obtained complexes of copper with o-hydroxybenzene-azo-β-naphthol and with o-carboxybenzeneazo-β-naphthol of the 1: 1 composition; in the same conditions we obtained the previously undescribed copper complex of o-carboxymethoxybenzeneazo-β-naphthol* of the 1: 1 composition.

By reacting copper chloride with o-methoxybenzeneazo-β-naphthol in conditions similar to those indicated above for the preparation of copper complexes of o,o'-disubstituted azo compounds, we obtained a new complex of 1: 1 composition differing both in composition and properties from the complex obtained by the previous investigators [2,6,8] from the same azo compound. We obtained a similar complex (1: 1 composition) also from 1-phenyl-3-methyl-4-(o-methoxybenzeneazo)-5-pyrazolone. Treatment of the prepared complexes with aqueous ammonia converts them into 1: 2 complexes identical with those obtained in the working conditions of Crippa [6]; the interaction is accompanied by loss of one atom of copper and two atoms of chlorine per 2 molecules of initial complex. Mineral acids decompose these complexes with separation of the original dyes.

Azo compounds from o-chloroaniline and o-nitroaniline, as diazo components, and β-naphthol and 1-phenyl-3-methyl-5-pyrazolone, as azo components, do not form 1: 1 complexes with copper. Their complexes with copper of the 1: 2 composition are formed smoothly.

On the basis of the properties of the prepared copper salts of o-hydroxy-o'-methoxyazo compounds with 1: 1 composition (absence of ionized copper, positive though weak reaction for chlorine ion, their transformation into 1: 2 complexes, formation of the original azo compounds by the action of mineral acids), of the data of elementary analysis, of the impossibility of formation of analogous compounds from o-chloro-and o-nitro-o'-hydroxyazo compounds and of general theoretical considerations, we can assign to the compound of o-methoxybenzeneazo-β-naphthol with copper the structure represented in the following scheme:



An analogous structure may be assigned to the copper compound of 1-phenyl-3-methyl-4-(o-methoxybenzene-azo)-5-pyrazolone.

* Although it is known [11] that the group of o-carboxymethoxy-o'-hydroxyazo compounds is susceptible to complex formation, the corresponding complexes have not been prepared in the pure state or analyzed.

TABLE 4

Absorption Maxima and Copper Numbers of Solutions of Biuret Complexes of Proteins and Gramicidin

Protein	Absorption maxima (in mμ)	Each mole copper requires protein (in g)		
		Calculated	Found	
			by M.I. Plekhan	by us
Sturin sulfate	540	691.4	-	691;683
Blood albumin	550	463.6	394	453;462
Hamersten's casein	550-555	532.0	570	568;569
Gliadin	555	520	-	559;576
Edestin	555	486	-	486;489
Gelatin	565	383.6	547	489;487
Gramicidin	535	643	-	646

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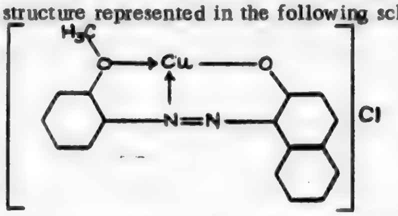

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* Although it is known [11] that the group of o-carboxymethoxy-o'-hydroxyazo compounds is susceptible to complex formation, the corresponding complexes have not been prepared in the pure state or analyzed.

EXPERIMENTAL

The starting monoazo compounds were prepared by the usual route, recrystallized from glacial acetic acid, washed with ethanol and identified from the melting points.

The C, H and N contents of the complexes were determined by elementary microanalysis; for determination of the content of Cu, Cl and azo compound in the complexes, the latter were decomposed with sulfuric acid, the dye was filtered off on a Schott funnel, and the copper in the filtrate was determined iodometrically and the chlorine by Mohr's method.

Copper salt of o-carboxymethoxybenzeneazo-β-naphthol. The azo compound from o-amino-phenoxyacetic acid (prepared by Thate's method [12] in the form of the potassium salt) and β-naphthol was obtained by coupling the components in an alkaline medium in very dilute solutions. Red needles soluble in organic solvents, sparingly soluble in water, m.p. 242°.

6.362 mg sub.: 15.536 mg CO_2; 2.346 mg H_2O. 3.204 mg sub.: 0.242 ml N_2 (22.5°, 738.2 mm). Found%: C 66.64; H 4.12; N 8.47. $C_{18}H_{14}O_4N_2$. Calculated %: C 67.08; H 4.35; N 8.69.

To a hot ethanolic solution of the azo compound was added an ethanolic solution of copper chloride, and the mixture was left to crystallize. The separated copper salt was washed with hot ethanol. Brown needles not melting up to 360°.

4.588 mg sub.: 9.480 mg CO_2; 1.272 mg H_2O. 3.056 mg sub.: 0.210 ml N_2 (22.4°, 737.8 mm). 0.2567 g sub.: 6.63 ml 0.1 N $Na_2S_2O_3$. Found %: C 56.43; H 3.11; N 7.71; Cu 16.42. $C_{18}H_{12}O_4N_2Cu$. Calculated %: C 56.31; H 3.13; N 7.30; Cu 16.57.

Copper salt of methoxybenzeneazo-β-naphthol (1:1). Prepared in the conditions of the preceding experiment Fine, brown needles not melting when heated to 360°.

6.338 mg sub.: 12.607 mg CO_2; 2.090 mg H_2O. 3.705 mg sub.: 0.288 ml N_2 (24°, 726 mm). 0.3830 g sub.: 10.09 ml 0.1 N $Na_2S_2O_3$. 0.5162 g sub.: 13.91 ml 0.1 N $AgNO_3$. Found%: C 54.28; H 3.69; N 8.53; Cu 16.75; Cl 9.57. $C_{17}H_{13}O_2N_2ClCu$. Calculated %: C 54.24; H 3.46; N 8.22; Cu 16.90; Cl 9.44.

It was decomposed by sulfuric acid to form the original dye with m.p. 177.5-178° (no depression of melting point in mixed test).

On shaking with an alcoholic solution of ammonia it is transformed into a crystalline substance with m.p. 221.5-222°, not giving a melting point depression with the substance obtained in Crippa's [6] working conditions and having a 1:2 composition.

0.3186 g sub: 5.19 ml 0.1 N $Na_2S_2O_3$; 0.2857 g azo compound. Found%: Cu 10.33; azo compound 89.67. $(C_{17}H_{13}O_2N_2)_2Cu$. Calculated %: Cu 10.29; azo compound 90.02.

Interaction is accompanied by separation of copper and chlorine, as indicated by the blue coloration of the solution characteristic of cuprammonium and by a definite reaction for chlorine with $AgNO_3$.

Copper salt of 1-phenyl-3-methyl-4-(o-methoxybenzeneazo)-5-pyrazolone (1:1). Prepared in the conditions of the preceding experiments but in a methanolic medium. Greenish-yellow hair-like needles, not melting up to 360°.

5.708 mg sub.: 10.592 mg CO_2; 1.832 mg H_2O. 2.800 mg sub.: 0.358 ml N_2 (29°, 729.5 mm). 0.2944 g sub.: 7.24 ml 0.1 N Na_2SO_3. 0.5778 g sub.: 14.47 ml 0.1 N $AgNO_3$. Found %: C 50.[illegible]; H 3.59; N 13.85; Cu 15.63; Cl 8.89. $C_{17}H_{15}O_2N_4ClCu$. Calculated %: C 50 23; H 3.69; N 13.78; Cu 15.65; Cl 8.74.

On heating with an aqueous ethanolic solution it is transformed into another modification – a dark, microcrystalline precipitate (fine greenish-yellow prisms under the microscope) with unchanged composition as confirmed by elementary analysis.

When both of these compounds (1:1 composition) are heated with ethanolic solution of ammonia they are transformed into the 1:2 complex. Brownish crystals with m.p. 285° (with decomp).

6.210 mg sub.: 13.784 mg CO_2; 2.396 mg H_2O. 3.414 mg sub.: 0.528 ml N_2 (29°, 718.2 mm). 0.4958 g sub.: 7.28 ml 0.1 N $Na_2S_2O_3$. Found %: C 60.57; H 4.32; N 16.48; Cu 9.35. $(C_{17}H_{15}O_2N_4)_2Cu$. Calculated %: C 60.21; H 4.43; N 16.53; Cu 9.38.

On interaction of the azo compounds from o-chloroaniline and o-nitroaniline and β-naphthol and 1-phenyl-3-methyl-5-pyrazolone with copper chloride in the conditions of the preceding experiments for preparation of 1:1 complexes, complex formation was not observed; on boiling ethanolic solutions of the above azo compounds with

copper chloride and aqueous ammonia solution, the corresponding 1:2 complexes were obtained.

Copper salt of o-chlorobenzeneazo-β-naphthol. Dark, coalescent platelets (under the microscope) with a greenish tinge, m.p. 232° (decomp.).

0.3154 g sub: 4.94 ml 0.1 N $Na_2S_2O_3$; 0.2840 g azo compound. Found %: Cu 9.96; azo compound 90.04. $(C_{16}H_{10}ON_2Cl)_2Cu$. Calculated %: Cu 10.15; azo compound 90.17.

Copper salt of o-nitrobenzeneazo-β-naphthol. Reddish-brown rods (under the microscope) with a greenish tinge, m.p. 264 (decomp.).

0.2010 g sub.: 3.12 ml 0.1 N $Na_2S_2O_3$; 0.1815 g azo compound. Found %: Cu 9.85; azo compound 90.28. $(C_{16}H_{10}O_3N_3)_2Cu$. Calculated %: Cu 9.82; azo compound 90.43.

Copper salt of 1-phenyl-3-methyl-4-(chlorobenzeneazo)-5-pyrazolone. Lustrous brown plates, m.p. 263° (decomp.).

0.2852 g sub.: 4.24 ml 0.1 N $Na_2S_2O_3$; 0.2588 g azo compound. Found %: Cu 9.45; azo compound 90.74. $(C_{16}H_{12}ON_4Cl)_2Cu$. Calculated %: Cu 9.26; azo compound 91.03.

Copper salt of 1-phenyl-3-methyl-4-(o-nitrobenzeneazo)-5-pyrazolone. Dark-brown prisms, partly coalescent, m.p. 248° (decomp.).

0.2822 g sub.: 4.00 ml 0.1 N $Na_2S_2O_3$; 0.2578 g azo compound. Found %: Cu 8.77; azo compound 91.36. $(C_{16}H_{12}O_3N_5)_2Cu$. Calculated %: Cu 8.98; azo compound 91.29.

All the prepared complexes are quickly decomposed by conc. sulfuric acid to form the original components, and they possess varying stabilities to the action of dilute acids; they are insoluble or poorly soluble in water, soluble in organic solvents, especially readily in chloroform and carbon bisulfide.

SUMMARY

1. Preparation and identification were carried out of new complexes of copper with azo compounds from o-aminophenoxyacetic acid, o-methoxyaniline, o-chloroaniline, and o-nitroanilines as diazo components, and β-naphthol and 1-phenyl-3-methyl-5-pyrazolone as azo components.

2. A possible structure is proposed for the copper complex of o-methoxybenzeneazo-β-naphthol and 1-phenyl-3-methyl-4-(o-methoxybenzeneazo)-5-pyrazolone with 1:1 composition.

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CONCERNING β-NITROVINYL-5-SUBSTITUTED FURANS

Z.N. Nazarova

The versatile properties of 2-furaldehyde permit its extensive utilization for a variety of syntheses and the preparation of a series of interesting and useful products [1].

It is know that substituents like chlorine, bromine and the nitro group increase the stability of the furan nucleus and intensify its bacteriostatic properties. In this connection great interest attaches to the as yet little studied 5-substituted 2-furaldehydes on whose basis can be obtained pharmacologically active substances [2] and insecticides [3].

The possibility of obtaining 5-substituted 2-furaldehydes (chloro-, bromo- and nitro- derivatives) was demonstrated by Gilman[3a]; however, the yield of the respective products was small. A new method for nitration of 2-furaldehyde was recently developed [4] which enabled the preparation from 5-nitro-2-furaldehyde of a series of nitrofuran derivatives possessing valuable bacteriostatic properties. We have shown [5] the possibility of preparation of 5-bromo-2-furaldehyde by direct bromination of 2-furaldehyde in dichloroethane in presence of traces of sulfur and hydroquinone in a yield of 60% of the theoretical.

Very little study has been devoted to condensations with bromo-2-furaldehyde; a series of syntheses described in the literature [6] nevertheless show that the presence of bromine in the furan nucleus does not in the majority of cases hinder the reactivity of the carbonyl group although it increases the stability of the furan ring. All condensations with bromo-2-furaldehyde proceed readily and with good yields of products.

Condensations of 5-bromo- and 5-nitro-2-furaldehyde with nitroparaffins have not previously been described in the literature. We carried out the condensation of 5-bromo-and 5-nitro-2-furaldehyde with nitromethane and chloronitromethane in the conditions described for condensation of 2-furaldehyde with chloronitromethane [7] and obtained: 5-bromofurylnitroethylene (92%); 5-bromofurylchloronitroethylene (83%); 5-nitrofurylnitroethylene (50%); and 5-nitrofurylchloronitroethylene (41%). It should be mentioned that the condensations with bromo-2-furaldehyde proceed with considerablry greater facility than with nitro-2-furaldehyde.

5-Bromofurylnitroethylene (see the scheme: I, A = H), obtained by us for the first time, forms lustrous yellow leaflets with m.p. 117-118° (from ethanol), easily soluble in organic solvents; it distils with steam and possesses an irritant action.

Although furylnitroethylene has been known for a long time [8], its bromination has not previously been studied. We brominated furylnitroethylene both in glacial acetic acid and in CCl_4 with heating and obtained a product with m.p. 117-118°, identical with the 5-bromofurylnitroethylene obtained as described above.

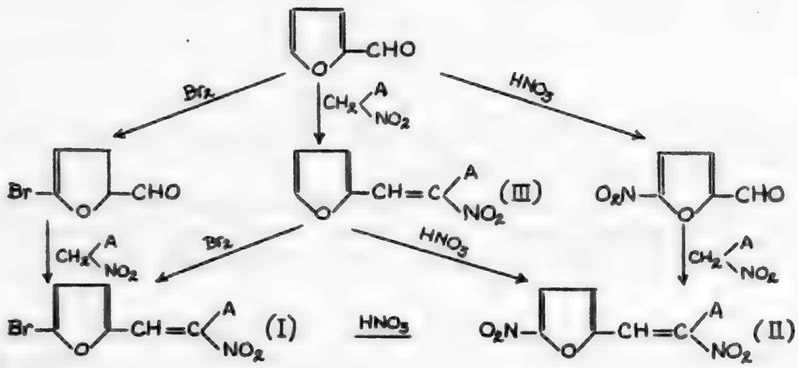
The 5-nitrofurylnitroethylene (II, A = H), obtained by us by direct synthesis, was identical with the product of nitration of furylnitroethylene previously described by Priebs [8] and forms yellow needles (from ethanol) with m.p. 142-143°.

In the course of study of the properties of the product of condensation of chloronitromethane with 2-furaldehyde, Tsukervanik and Potemkin [7] studied the bromination and nitration of furylchloronitroethylene (III, A = Cl) and obtained respectively a bromination product with m.p. 74-75° and a nitration product with m.p. 83-84°. On the basis of literature data and of the transformation of the bromo- into the nitro- derivative under the action of nitric acid (d 1.2) the authors assumed that the most probable structures were 5-bromo- and 5-nitro-substituted β-nitrovinylfurans. A direct comparison by us showed that these products were actually 5-bromofurylchloronitroethylene and 5-nitrofurylchloronitroethylene, which we prepared by condensation of 5-bromo- and 5-nitro-2-furaldehydes with chloronitromethane.

It is interesting to note the interchangeability of the 5-bromo derivatives with the corresponding 5-nitro derivatives: on heating 5-bromofurylnitroethylene and 5-bromofurylchloronitroethylene with nitric acid, 5-nitrofurylnitroethylene and 5-nitrofurylchloronitroethylene, respectively, are formed: the bromine atom in the 5-position is replaced by a nitro group with liberation of free bromine. Similar exchange reactions of halogen in the furan nucleus have been described in the literature [7]. In these conditions bromo-2-furaldehyde does not give nitro-2-furaldehyde.

The fact has thus been verified that bromination of β-nitrovinylfurans is not accompanied by addition of bromine at the double bond of the side chain, but that in the first instance the α-hydrogen in the furan nucleus is substituted; nitration likewise yields 5-nitro-substituted β-nitrovinylfurans.

All the transformations described above are summarized in the scheme.



where: A=H,Cl.

EXPERIMENTAL

5-Bromo-2-furaldehyde [5]. To a solution of 28.8 g (0.3 mole) 2-furaldehyde * in 120 ml dichloroethane was added 0.005 g each of sulfur and hydroquinone and with heating on a water bath (reflux condenser with a lead-off tube at the end) addition was made from a dropping funnel of a solution of 57.5 g (0.32 g-mole) bromine in 150 ml dichloroethane at such a speed that the Br entered into reaction. After all the bromine had been added (3 hours), heating was contined until hydrogen bromide ceased to be evolved (about 3 hours). The reaction mixture was then steam distilled. After the solvent had been driven off, yellowish crystals of bromo-2-furaldehyde appeared in the condenser. The bromo-2-furaldehyde was collected, washed with cold water and dried. Yield 32 g (60.7%). The crude product had m.p. 79-80°. Recrystallization from 50% ethanol gave colorless needles with m.p. 82°.

5-Nitro-2-furaldehyde was obtained by nitration of 2-furaldehyde with nitric acid (d 1.52) in presence of acetic anhydride, followed by saponification of the nitro-2-furaldehyde diacetate with sulfuric acid [9].

Chloronitromethane was prepared by Chernyak's method [10] of chlorination of the sodium salt of nitromethane.

I. 5-Bromofurylnitroethylene

Prepared by two methods. a) Condensation of nitromethane with bromo-2-furaldehyde. To a well-cooled (ice and salt) solution of 3.5 g (0.02 mole) bromo-2-furaldehyde and 1.62 g (0.026 mole) nitromethane in 15 ml methanol was added, dropwise with shaking, a solution of 0.8 g (0.02 mole) NaOH in 5 ml water. The conclusion of addition of the alkali was followed by separation of a voluminous precipitate of the sodium salt of bromofurylnitroethanol. The mixture was left for 20 minutes in a freezing mixture, after which water with ice was added to dissolve the precipitate (about 20 ml). With vigorous stirring the well-cooled mixture was run dropwise into 7 ml 10% hydrochloric acid (cooled to -5°) at such a rate that the temperature did not rise above 0°. The precipitate was separated, washed with cold water and distilled with steam. Yield of yellow crystals with m.p. 116-118° 4 g (92%); recrystallization from ethanol gave yellow platelets with m.p. 117-118°, readily soluble in organic solvents, insoluble in water.

0.0988 g sub.: 0.0855 g AgBr. Found %: Br 36.82. $C_6H_4O_3NBr$. Calculated %: Br 36.70.

b) Bromination of furylnitroethylene.** Furylnitroethylene, prepared in a similar manner by condensation of 2-furaldehyde with nitromethane in a yield of 77% (m.p. 74-75°), was brominated in the conditions described for bromination of ethyl-α-cyano-β-furylacrylate [6b]. To a solution of 2 g (0.014 mole) furylnitroethylene in 7.5 ml hot glacial acetic acid was added dropwise a solution of 2.5 g (0.014 mole) bromine in 3 ml glacial acetic acid. The mixture was refluxed until cessation of evolution of HBr (about 1 hour); after cooling, the solution was diluted with water and the resultant precipitate was separated, washed with water and steam distilled. The crystals which came over were twice recrystallized from ethanol – yellow leaflets with m.p. 117-118°. No melting point depression

* Technical 2-furaldehyde was purified by washing with Na_2CO_3 solution (10%) and cold water, drying with Na_2SO_4 and distilling in a column (12 theoretical plates), b.p. 159° (727 mm). The bromine and dichloroethane were dried over calcined $CaCl_2$.

** With participation of Bugrova.

in admixture with 5-bromo-furylnitroethylene. The same product with m.p. 117-118° was isolated after bromination of furylnitroethylene in CCl_4.

II. 5-Nitrofurylnitroethylene

Obtained by three methods. a) Condensation of nitro-2-furaldehyde with nitromethane was carried out in a similar manner to the condensation of bromo-2-furaldehyde. Components were 2.8 g (0.02 mole) nitro-2-furaldehyde, 1.22 g (0.02 mole) nitromethane, 5 ml methanol, 1 g NaOH in 5 ml water and 7 ml 10% hydrochloric acid. A precipitate did not appear when caustic alkali solution was added and no crystals separated when poured into cooled hydrochloric acid, but an oil formed which solidified only after dilution with water and prolonged shaking. After two recrystallizations from ethanol, orange-yellow crystals were obtained with m.p. 142-143°.

Nitrofurylnitroethylene is not volatile in steam; it is soluble in organic solvents; with caustic alkalies it gives a deep-colored solution which rapidly darkens.

b) Interaction of bromofurylnitroethylene with nitric acid. A mixture of 2.18 g (0.01 mole) bromofurylnitroethylene and 7 ml nitric acid (d 1.2) was heated until an exothermic action commenced to the accompaniment of evolution of free bromine. The bromonitrofurylethylene completely dissolved. The mixture was diluted with water, neutralized with $NaHCO_3$ solution and extracted with ether. From the ethereal solution isolated yellow crystals which after two recrystallizations from ethanol melted at 142-143° and did not contain halogen. A mixed test with 5-nitrofurylnitroethylene did not give a depression of melting point.

c) Nitration of furylnitroethylene. To 8.35 g (0.13 mole) nitric acid (d 1.52) with cooling (not above -5°) was gradually added (in the course of 0.5 hour with mechanical stirring) 2 g (0.014 mole) furylnitroethylene. After all had been added (the mixture solidified) addition was made of 5 ml glacial acetic acid and the stirring was continued for another 2 hours at 0°. The whole mass was then poured into 70 ml crushed ice; 15 minutes later the precipitate was separated, washed with water and dried between sheets of filter paper. Yield of crude product 2.6 g (98%), m.p. 132-134°. Recrystallization from ethanol gave 1.6 g (60.54%) yellow-orange crystals with m.p. 142-143°. A mixed test with 5-nitrofurylnitroethylene did not give a depression of m.p.

III. 5-Bromofurylchloronitroethylene

Condensation of bromo-2-furaldehyde with chloronitromethane. Components were 3.5 g (0.02 mole) bromo-2-furaldehyde, 1.9 g (0.02 mole) chloronitromethane, 15 ml methanol, 0.8 g (0.02 mole) NaOH in 5 ml water and 7 ml 10% hydrochloric acid. Condensation was effected as in the preceding experiments. After pouring into the hydrochloric acid, the reaction mixture was steam distilled to give yellow crystals with m.p. 65-68°. Recrystallization from ethanol gave bright-yellow, lustrous (mother-of-pearl) leaflets with m.p. 74.75°. Yield 4.2 g (83%). A mixed test with the product of bromination of furylchloronitroethylene [7] did not give a depression of melting point.

IV. 5-Nitrofurylchloronitroethylene

a) Condensation of 5-nitro-2-furaldehyde with chloronitromethane. Materials used were 2.3 g (0.02 mole) nitro-2-furaldehyde, 1.9 g (0.02 mole) chloronitromethane, 10 ml methanol, 1 g NaOH in 5 ml water and 7 ml 10% hydrochloric acid. Addition of the alkali brought down a small precipitate and a heavy oil which solidified after dilution with water and prolonged shaking in a freezing mixture. Extraction with ether gave 1.5 g (41.4%) crystalline mass. Two recrystallizations from ethanol gave orange-yellow crystals with m.p. 83-84°. A mixed test with the product of nitration of furylchloronitroethylene [7] did not give a depression of melting point.

b) Reaction of 5-bromofurylchloronitroethylene with nitric acid (d 1.2) yielded crystals with m.p. 83-84°. A mixed test with 5-nitrofurylchloronitroethylene did not give a depression of melting point.

SUMMARY

1. For the first time the condensation was effected of 5-bromo- and 5-nitro-2-furaldehydes with nitromethane and chloronitromethane to give respectively 5-bromofurylnitroethylene (not described in the literature), 5-bromofurylchloronitroethylene, 5-nitrofurylnitroethylene, and 5-nitrofurylchloronitroethylene.

2. It was demonstrated that in the bromination and nitration of furylnitroethylene and furylchloronitroethylene the α-hydrogen of the furan ring is substituted with formation of the 5-bromo and the 5-nitro derivative respectively.

3. It is shown that treatment of 5-bromo-(β-nitrovinyl)-furans with nitric acid converts them into the corresponding 5-nitro derivatives with release of free bromine. In these conditons bromo-2-furaldehyde does not give nitro-2-furaldehyde.

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IN MEMORY OF EVGENY ALEKSEEVICH IVANOV

On January 27, 1953, after a long and serious illness passed away Evgeny Alekseevich Ivanov, head of the central laboratory of the Dorogomilovsk M.V. Frunze Chemical Works, member of the Scientific Council of the K.E. Voroshilov Research Institute for Intermediates and Dyes, Stalin Laureat, one of the leading workers of the aniline dye industry.

E.A. Ivanov was born in 1903 at Saratov in the family of a state teacher. After leaving the intermediate school he went to the Moscow G.V. Plekhanov Institute of National Economy which he left in 1929 with the diploma of engineering technologist. From that time his working life was spent at the Dorogomilovsk Works where he progressed from shift manager to research manager and then to control of the central laboratory. Here E.A. Ivanov completed more than 50 original investigations. These were not remote from practical matters and many of them served as a basis for the organization at the Dorogomilovsk Works of a series of manufactures of intermediates and dyes introduced for the first time to our industry.

Among a number of researches on the larger scale carried out by E.A. Ivanov or under his direction and later adopted by the works, mention should be made of the development of procedures for the manufacture of: p-nitro-o-anisidine, p-toluenesulfochloride, the nitrotoluidines, p-toluidine disulfonic acid, quinizarin, and a series of acid anthraquinone dyes.

We must also put on record the great and carefully executed investigation by E.A. Ivanov of the mechanism and kinetics of formation of dialkylamines from nitrosodialkylanilines.

Under the direction of E.A. Ivanov important studies were initiated by the Dorogomilovsk works collective on the new technology of production of diphenylguanidine and a series of other products. In later years E.A. Ivanov with a large collective undertook important studies which foresaw a change in the technology of production of a series of large-scale intermediates of the aniline dye industry, with the aim of improving the hygienic conditions of operation. For his part in this project, whose results were adopted by the industry, he was granted the title of Stalin Laureate in 1951.

The economic effect of the results of E.A. Ivanov's researches can be reckoned in millions of rubles.

Since 1949 E.A. Ivanov was a member of the Communist Party of the Soviet Union. For his services he was honored with the Order of Worker of the Red Banner, with medals "For Working Valor",, "For Valiant Work in the Great Patriotic War," and "In Memory of 8 Centuries of Moscow".

E.A. Ivanov was a sensitive and sympathetic man and won the affection and respect of his working comrades. His premature death has cut short his life in the plenitude of his powers.

V.M. Rodionov, N.N. Vorozhtsov, A.F. Smirnova,
L.A. Shchetinina,
A.P. Shestov, A.I. Korolev, V.O. Lukashevich,
V.N. Ufimtsev

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